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FOREWORD

The *United States Armed Forces Medical Journal* is the medium for disseminating information of administrative and professional interest to all medical personnel of the Department of Defense. The Chairman of the Armed Forces Medical Policy Council and the Surgeons General of the several services invite all medical officers, dental officers, Medical Service Corps officers, Nurse Corps officers, and officers of the Veterinary Corps of the Armed Forces, and the medical consultants of the Army, Navy, and Air Force to submit manuscripts for publication in this *Journal.*

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The summary should be a factual and brief recapitulation of the observations or statements contained in the article. The conclusions drawn from the case, experiment, or facts set forth should be clearly stated and should appear at the close.

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All original contributions are accepted on the assumption that they have not appeared previously and are not to be reprinted elsewhere without the permission of the editor of this *Journal* and that editorial privilege is granted to the editor in preparing all material submitted for publication. Authors are urged to keep their articles short.

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Monthly Message

Since early times warriors have used protective devices ranging from the simple shield of the jungle savage to the complicated total body armor of the knights of the Middle Ages. The relatively stable trench warfare of World War I was symbolized by the steel helmet, whereas the more fluid and mobile combat actions observed in recent hostilities have resulted in the development of group protective body armor as exemplified by the modern tank or the encircling steel apron of the naval gun as well as the individual protective flak vests of our airmen.

Studies in wound ballistics reveal that a rather constant major proportion of body injuries incurred in combat are due to shell fragments. Comparisons of body area wound statistics of the Korean conflict with those of World War II show only minor variations and reveal that about 20 percent of the wounds incurred in action are caused by high velocity missiles, the remaining 80 percent being the result of lower velocity shell fragments. About 25 percent of those wounded in action sustain injuries of the chest and abdomen. In this portion the ultimate case fatality rate is much higher and many more hours of valuable surgical team time are required per case than in the 60 percent incurring wounds of the extremities.

Any further reduction in the casualty rate must lie in the use of some type of body armor. The Armed Forces Medical Policy Council has been keenly interested in the development of a practical protective element of value to those exposed to the hazards of open combat and has given policy support to the tests of body armor being conducted by the Marines in Korea. Certain minor problems, such as the adequacy of body area coverage, the possibility of further reduction in weight, and the generation of excessive body heat, are in the process of solution. This added protective equipment has been well received by the combat soldier as reflected in the reply of a marine in combat, when querried about wearing it even with the temperature well over 100° F., "Doc, I'd rather drip sweat than drip blood."

Melvin A. Casberg

Melvin A. Casberg, *M. D., Chairman*
Armed Forces Medical Policy Council
Office of the Secretary of Defense

OXYGEN VS. OXYGEN-CARBON DIOXIDE IN RESUSCITATION[1]

DAVID B. DILL, *Ph. D.*

THE advisability of adding carbon dioxide to oxygen for resuscitation has been debated for more than 30 years. In the case of resuscitation from carbon monoxide poisoning an affirmative recommendation was made in 1923 by a Commission appointed at the request of the American Gas Association (2). The Commission was composed of 9 eminent physiologists and experts in clinical medicine, including as chairman, C. K. Drinker. Two of the physiologist members, Henderson and Haggard, had advocated the use of such a mixture for several years prior to the authoritative endorsement by the Commission. The Commission condemned the "pulmotor" and "lungmotor," preferring manual artificial respiration by the Schafer prone pressure method, if breathing had stopped. The Henderson-Haggard "inhalator," using 5 percent carbon dioxide in oxygen, was approved (3).

Although some members of the Commission subsequently reached different conclusions, Henderson never wavered. His vigorous arguments were reiterated in 1938 (4) and again in 1943 (5). The most desirable concentration of carbon dioxide was investigated by Drinker and his associates. The results, summarized by Drinker (6), led to the adoption of 7 percent carbon dioxide in oxygen. This mixture has become known as "carbogen."

The past 10 years have seen notable advances in the field of artificial respiration. A new manual method has been adopted in this country (7), and several mechanical devices have come into

(1) From the Chemical Corps Medical Laboratories, Army Chemical Center, Md.

(2) Drinker, C. K.; Cannon, W. B.; Edsall, D. L.; Haggard, H. W.; Henderson, L. J.; Henderson, Y.; Peabody, F. W.; Sayers, R. R.; and Scott, C. B.: Final report of commission on resuscitation from carbon monoxide asphyxia; treatment of carbon monoxide asphyxia. J. Industrial Hygiene 5: 125-129, 1923-1924.

(3) This apparatus is manufactured by the Mine Safety Appliances Company.

(4) Henderson, Y.: Adventures in Respiration. Williams & Wilkins Co., Baltimore, Md., 1938.

(5) Henderson, Y., and Haggard, H. W.: Noxious Gases and the Principles of Respiration Influencing Their Action. 2d edition. Reinhold Publishing Corporation, New York, N. Y., 1943.

(6) Drinker, C. K.: Carbon Monoxide Asphyxia. Oxford University Press, New York, N. Y., 1938.

(7) Dill, D. B.: Manual artificial respiration. U. S. Armed Forces M. J. 3: 171-184, Feb. 1952.

use. In 1944 the Council of Physical Medicine of the American Medical Association published the following *(8)*:

"Included in the Council's list of accepted devices are inhalators and resuscitators, the two types of apparatus for administering mechanical artificial respiration. These devices are often confused as to function; the following briefly describes them:

"Inhalators provide an atmosphere of oxygen and carbon dioxide gas mixture slightly higher than atmospheric pressure around the mouth and nose of the victim and are used in conjunction with an approved method of manual artificial respiration. Inhalators consist essentially of a face piece, rubberized fabric breathing bag, pressure reducing valve, tanks of carbon dioxide-oxygen mixture and carrying case.

"Resuscitators create (either) positive and negative pressure by means of a mechanical appliance operated by the energy of the stored gas (or) merely (intermittent) positive pressure only. A face piece, reduction valve, tanks of carbon dioxide-oxygen mixture or merely tanks of oxygen, a carrying case, and a reciprocating mechanism are the principal parts of the resuscitator.

"The efficacy of the two types of appliances has been shown to be essentially the same by the evidence coming to the Council. Records show that when an inhalator and a resuscitator are on the scene of an accident at the same moment, and if either one is employed efficiently, the final result will not differ."

During this 10-year period many experts in anesthesia have come to doubt the soundness of adding carbon dioxide to oxygen for resuscitation, even in carbon monoxide poisoning. In 1947 Adriani *(9)* made the following recommendation:

"Do not add carbon dioxide to the oxygen mixture. The use of carbon dioxide for respiratory failure is a controversial subject. Do not worry if it is not available. Oxygen is the gas which must be introduced into the alveoli."

COMPARISON OF OXYGEN AND CARBOGEN

It remained for Schwerma et al. *(10, 11)* to settle some of these questions beyond reasonable doubt. In one study *(10)* 310 dogs

(8) Artificial respiration—manual and mechanical; report of Council on Physical Medicine. J. A. M. A. 126: 835, Nov. 25, 1944.

(9) Adriani, J.: Techniques and Procedures of Anesthesia. Charles C Thomas, Publisher, Springfield, Ill., 1947.

(10) Schwerma, H.; Ivy, A. C.; Friedman, H.; and LaBrosse, E.: Study of resuscitation from juxtalethal effects of exposure to carbon monoxide. Occup. Med. 5: 24-48, Jan. 1948.

(11) Schwerma, H.; Ivy, A. C.; and Friedman, H.: Resuscitations from nearly fatal effects of exposure to "pure" carbon monoxide. J. Appl. Physiol. 1: 157-168, Aug. 1948.

were poisoned to the point of gasping respiration with illuminating gas diluted with air and in a similar study *(11)* on 157 dogs, commercial carbon monoxide diluted with air was used. Two types of mechanical devices (positive-negative and intermittent positive) were used for resuscitation. With the former both oxygen and carbogen were evaluated; with the latter only carbogen was used. The authors concluded that 100 percent oxygen and carbogen were equal in effectiveness. This conclusion was valid for 2 criteria of success (immediate survival and incidence of neurologic injury). The number of dogs used insured statistical validity.

Expert opinion. Many physiologists have entered the field of anesthesiology in recent years. They have played a major role in strengthening this science and in narrowing the gap between research in respiratory physiology and its applications in the operating room and in the emergency ward. Hence it seemed appropriate to inquire regarding the use of carbogen in artificial respiration. Such an inquiry was addressed to a number of respiratory physiologists and to several anesthesiologists. Several of both groups have been associated under contract with the military Medical Services or the Chemical Corps in research in the field of respiratory physiology. Excerpts of the views expressed follow:

John S. Gray, Chairman, Department of Physiology, The Medical School, Northwestern University: "* * * it is certainly the opinion of our Physiology Department that pure oxygen is a great deal safer for general resuscitative uses than carbon dioxide-oxygen mixtures. The reasons for this opinion are numerous. In cases where resuscitation is essential, namely, when breathing has stopped entirely, or is quite feeble, anoxemia, hypercapnia, and acidemia (both respiratory and metabolic) are all present. This combination is especially dangerous, because in the presence of respiratory center depression (from oxygen lack certainly, and severe acidemia probably) the hypercapnia is converted to a respiratory *inhibitor* instead of a stimulator (the well-known "carbon dioxide reversal"). This inhibition by depressing respiration further, exaggerates the 3 changes, so that a vicious cycle is set up, which runs a rapidly fatal course. The objective of resuscitation should be to break this vicious cycle, and reverse the chemical disturbances. The inclusion of carbon dioxide in the inhaled mixture at best interferes with this objective, and at worst aggravates the problem. Furthermore, if spontaneous breathing is restored, the body's normal compensation for the surviving metabolic acidosis is to produce acapnia to minimize the pH shift; this objective of nature is likewise interfered with by the inclusion of carbon dioxide. The gradual recognition of the above facts, together with the gradual recog-

nition of the fact that there was never experimental evidence nor rationale to support the use of carbon dioxide in the first place, has lead to a gradual abandonment of the use of carbon dioxide for general resuscitative purposes.

"Opinion is less well crystallized with respect to the use of carbon dioxide in the respiratory *support* (not restoration of breathing after apnea) in case of carbon monoxide poisoning. Here, there is a possibility that the augmented ventilation and respiratory acidosis may accelerate the elimination of carbon monoxide from the body. But this is an entirely different matter than true resuscitation. Even the carbon monoxide poisoning case, in the *acute* stage when resuscitation is required, should not be given carbon dioxide; in the recovery stage, it may be used to hasten elimination of the poison."

Robert D. Dripps, Professor of Anesthesiology, The Graduate School of Medicine, University of Pennsylvania: "We prefer 100 percent oxygen, believing that wherever respiratory tidal volume is depressed, arterial blood carbon dioxide will be increased and further addition of carbon dioxide may not only not be stimulant but may even be depressant to the central nervous system. In our own institution we do not even use carbon dioxide and oxygen combinations for the treatment of carbon monoxide poisoning. The only exception to the rule for use of 100 percent oxygen is when a subject does not breathe for many hours or days. Under these circumstances if 100 percent oxygen be administered for excessive lengths of time, oxygen toxicity may occur. We have had this experience in several neurosurgical patients who have required artificial ventilation for days. Under these circumstances we prefer 50 percent oxygen and 50 percent nitrogen."

Henry K. Beecher, Dorr Professor of Research in Anesthesia, Anesthetist-in-Chief, Department of Anesthesia, Massachusetts General Hospital, Harvard Medical School: "We use only oxygen here and have even gone so far as to banish carbon dioxide tanks from the emergency wards and operating rooms, lest there be an interchange of tanks, with disastrous results. We do not have the 95 percent oxygen-5 percent carbon dioxide mixtures either. It is my understanding that these percentages do not hold well as the pressure in the tank changes. But far more important than any of these reasons is the fact that we do not find the carbon dioxide necessary nor its use wise in the type of problem which comes into this rather large general hospital. Individuals in respiratory difficulty are almost always suffering (at least in the serious cases) from an excess of carbon dioxide in the tissues and blood. While the expert might occasionally find a rare use for carbon dioxide in conjunction with resuscitation, we do not believe that

it is really necessary nor wise to have it around in a place where we do so much teaching. This reason, of course, is pertinent to the problems that may arise when less than skilled personnel would presumably be carrying out such resuscitation in the event of a national disaster."

Max S. Sadove, Professor of Surgery, Head, Division of Anesthesiology, Research and Educational Hospitals, University of Illinois: "* * * one can easily do without carbon dioxide–oxygen mixtures. It is true that in some special, rare instances such as carbon monoxide poisoning, some have advocated the use of carbon dioxide–oxygen mixtures to aid in the dissociation of the carbon monoxide-hemoglobin link. But, even in these instances, one wonders whether 5 percent is correct, or 3 percent, or what percent is correct.

"I think that when carbon dioxide–oxygen is used, it should be used purely as a therapeutic procedure of an experimental nature or for a specific purpose, but certainly it has no place as a general vehicle for resuscitative measures. In most instances, there is already an excess of carbon dioxide in the body and the further addition of the carbon dioxide would probably do a great deal of harm rather than any good. I can visualize it depressing the central nervous system and in the higher concentrations it may be seen doing damage to the brain and the vascular bed as well."

"I personally would say that as a routine procedure, only oxygen should be attached to resuscitators. True, carbon dioxide may be used for its vasodilation in the cerebral cortex, it may be used intermittently to stimulate respiration, et cetera, but it has no place in the routine resuscitative procedures, with the one possible exception of carbon monoxide poisoning. There I would state that one would be better off having only oxygen available on resuscitators and those rare instances where carbon dioxide is used, attaching it for just that purpose."

Eugene F. DuBois, Emeritus Professor of Physiology, Cornell University Medical College: "Our chief anaesthetist * * * tells me that after operations he uses pure oxygen. He has given up 95-5 percent carbon dioxide mixture."

David Grob, Department of Medicine, The Johns Hopkins Hospital: "The procedure at the hospital is to use oxygen rather than oxygen-carbon dioxide mixtures for resuscitation purposes, with the possible exception of carbon monoxide poisoning in which the mixture is used in order to attempt to shift the pH of the blood to a more acid range, in order to increase the dissociation of carboxy-hemoglobin. The only other use of the mixture here has been to attempt to increase the depth of breathing transiently in

patients who are breathing voluntarily and in whom it is desired to expand the alveoli or encourage coughing, as in postoperative patients. In all anoxic or asphyxiated patients, particularly those who are not breathing voluntarily, oxygen is administered and there would seem to be no advantage to adding carbon dioxide. In patients with advanced emphysema it has, of course, been recently observed that prolonged breathing of pure oxygen may depress respiration. In such cases periods of breathing of room air are employed. I do not believe that the oxygen-carbon dioxide mixtures would be used in such patients as the concentration of carbon dioxide in the blood and alveoli is already higher than normal."

Wallace O. Fenn, Professor of Physiology, the University of Rochester, Strong Memorial Hospital, School of Medicine and Dentistry: "* * * in cases of asphyxia the carbon dioxide tension is already high and additional carbon dioxide would be expected to narcotize rather than to stimulate the respiratory center. Possibly for this reason the use of carbon dioxide in oxygen mixtures has been generally given up. Perhaps it should be recommended for resuscitation after carbon monoxide poisoning because it helps to eliminate carbon monoxide from the blood. I believe that Schwerma, Ivy, and others have also found no benefit from the use of carbon dioxide in practical tests of resuscitation."

David G. Greene, The University of Buffalo, School of Medicine, Buffalo General Hospital, Department of Medicine: "* * * with the possible exception of carbon monoxide poisoning, there is no rationale for adding carbon dioxide to oxygen in the gas used for resuscitation. The anesthetists here concur in this opinion."

Andre Cournand, Cardio-Pulmonary Laboratory, Bellevue Hospital, Chest Service, (Columbia University Division): "* * * I see no indication for the use of oxygen carbon dioxide mixtures in resuscitation with or without resuscitators. In my experience, high oxygen-nitrogen mixtures can be used with satisfaction for prolonged periods of time."

W. K. Nowill, Assistant Professor of Anesthesiology, Department of Surgery, School of Medicine, Duke University: "* * * general opinion is that 100 percent oxygen is proper for resuscitation in acute cases. For prolonged resuscitation, 50 to 70 percent oxygen with nitrogen or helium is thought to be better. Five percent carbon dioxide is used only in cases of carbon monoxide poisoning. However, the problems involved in resuscitation are far from being solved. The effect of carbon dioxide on body physiology during various types of asphyxial states are incompletely known."

Albert Faulconer, Section on Anesthesiology, Mayo Clinic: "* * * Common practice at the Mayo Clinic in resuscitation from cardio-respiratory failure includes the use of 100 percent oxygen. Oxygen with carbon dioxide added is not used for this purpose."

Joseph H. Holmes, Professor of Medicine, University of Colorado, Department of Medicine: "The group here do not use the carbon dioxide mixture but use 100 percent oxygen."

Jay Jacoby, Director of Anesthesia, University Hospital, The Ohio State University: "Oxygen is the preferred gas for resuscitation. Patients who require resuscitation already have built up an abnormally high blood carbon dioxide level, and it is not logical to administer more. Carbon monoxide poisoning is almost the only exception, since there is no increase of carbon dioxide in the blood, and a slight increase would be of some value, not as a respiratory stimulant, but in hastening the breakdown of carbon monoxide-hemoglobin combination."

DISCUSSION

The argument that in resuscitation the addition of carbon dioxide to oxygen will stimulate respiration was plausible. Unfortunately the issue was never resolved by adequate experiments until 1948 *(9, 10)*. In the one situation where carbogen would seem effective, carbon monoxide poisoning, no advantage was found in using the mixture for mechanical artificial respiration. In other situations the body may be flooded with an excess of carbon dioxide; the addition of more would not be useful and might be harmful. In nerve gas poisoning, for example, the diaphragm may be paralyzed; respiration stops and life depends on artificial respiration, continued until normal respiratory activity is re-established. Resuscitation can be accomplished with air alone, especially if atropine is used. Atropine's actions on the central and peripheral nervous systems and on effectors shorten the time required to restore breathing and diminish respiratory embarrassment by such factors as bronchial secretion. Oxygen is desirable, but mixing 7 percent carbon dioxide with it dams back the excess of carbon dioxide accumulated in the body.

CONCLUSIONS

In resuscitation from carbon monoxide poisoning the use of carbogen is of questionable value. In resuscitation from other forms of asphyxia its use may be harmful. Expert respiratory physiologists and anesthesiologists generally prefer 100 percent oxygen to carbogen in artificial respiration although some think the latter may be useful in treating asphyxia caused by carbon monoxide. Because the use of carbogen may be harmful in some types of asphyxia, there is danger in having both 100 percent

oxygen and carbogen available. Logistic considerations also argue against the use of both. It is recommended that the admixture of carbon dioxide with oxygen for artificial respiration be abandoned.

BOOKS RECEIVED

Dictionary of Civil Defence, Edited by *Carlton Wallace,* Associate Fellow Institute of Civil Defence. 160 pages; illustrated. Philosophical Library, New York, N. Y., publishers, 1952. Price $2.75.

Malignant Disease and its Treatment by Radium, Volume IV, by *Sir Stanford Cade,* K. B. E., C. B., F. R. C. S., M. R. C. P., F. F. R. (Hon.), Surgeon, Westminster Hospital; Consulting Surgeon, Mount Vernon Hospital and Radium Institute; Lecturer in Surgery, Westminster Medical School and formerly Examiner in Surgery, University of London; Member of the Council, late Hunterian Professor, Arris and Gale Lecturer and member of the Court of Examiners, Royal College of Surgeons of England; Hon. Member American Radium Society; Consultant in Surgery to the Royal Air Force, With a foreword by *Sir Ernest Rock Carling,* F. R. C. P., F. R. C. S., F. F. R., Consulting Surgeon and Vice-President, Westminster Hospital. 2d edition. 544 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1952.

Operative Neurosurgery, With Emphasis on Procedures in Trauma, by *Elisha Stephens Gurdjian,* M. D., Professor of Neurosurgery, Wayne University College of Medicine; Chief, University Neurosurgical Service, Grace Hospital, Detroit, Mich., and *John E. Webster,* M. D., Assistant Professor of Surgery, Wayne University College of Medicine; University Neurosurgical Service, Grace Hospital, Detroit, Mich. 422 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1952. Price $10.

Physics and Medicine of the Upper Atmosphere, A Study of the Aeropause, Edited by *Clayton S. White,* M. D., Director of Research, Lovelace Foundation for Medical Education and Research. Head of a Section of Aviation Medicine, Lovelace Clinic, and *Otis O. Benson,* Jr., Bragadier General, USAF (MC), Commandant, USAF School of Aviation Medicine. The Proceedings of a Symposium on the Physics and Medicine of the Upper Atmosphere held at San Antonio, Tex., November 6, 7, 8, 9, 1951, sponsored by The Air University School of Aviation Medicine, Randolph Field, Tex. Arranged by The Lovelace Foundation for Medical Education and Research, Albuquerque, N. M. 611 pages; illustrated. Published by the University of New Mexico Press, Albuquerque, 1952. Price $10.

Electrotherapy and Actinotherapy, A Textbook for Student Physiotherapists, by *E. B. Clayton,* M. B., B. Ch. (Cantab.), Consulting Physician to The Physical Treatment Department, King's College Hospital, London. 2d edition. 452 pages; illustrated. Published in the United States by The Williams & Wilkins Co., Baltimore, Md., publishers, 1952. Price $4.

THORACOABDOMINAL INCISION FOR RESECTION OF ADRENAL TUMORS[1]

R. MAURICE HOOD, *Lieutenant, MC, U. S. N.*

EVERETT H. DICKINSON, *Captain, MC, U. S. N.*

THE necessity for surgical resection of lesions of the adrenal gland is becoming quite common. This is attested to by the rather numerous reports appearing in the literature of the past 5 years *(2-6)*. Despite the work of Chute et al. *(7-9)* which points out the advantages of the thoracoabdominal approach to the kidney and the adrenal gland, this approach is not yet commonly used. Sweet *(10)* has stated that transthoracic incisions offer the best approach to the adrenal glands, and Grimson et al. *(5)* have used a transdiaphragmatic approach. Priestley et al. *(6)*, although admitting the superiority of the exposure, apparently favor a posterolumbar incision. Our experience, although limited, has clearly indicated the superiority of the thoracoabdominal exposure of the adrenal area.

The adrenal glands, though lying beneath the diaphragm, are well within the thoracic cage lying opposite the ninth and tenth ribs posteriorly. The surgical approach transperitoneally is characterized by difficult exposure chiefly because of the overlying liver on the right side and spleen, stomach, and pancreas

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(1) Surgical Service, U. S. Naval Hospital, Oakland, Calif.

(2) Mortensen, H., and Murphy, L.: Feminizing adrenal tumor in adult male. J. Urol. 65: 709-714, May 1951.

(3) Pyle, F. J.: Pheochromocytoma; report of malignant case (pheochromoblastoma). J. Urol. 66: 153-162, Aug. 1951.

(4) Garrett, R. A.: Adrenal cortical carcinoma in children. J. Urol. 66: 477-485, Oct. 1951.

(5) Grimson, K. S.; Emlet, J. R.; and Hamblen, E. C.: Diagnosis and management of tumors of adrenal gland. Ann. Surg. 134: 451-463, Sept. 1951.

(6) Priestley, J. T.; Sprague, R. G.; Walters, W.; and Salassa, R. M.: Subtotal adrenalextomy for Cushing's syndrome; preliminary report of 29 cases. Ann. Surg. 134: 464-475, Sept. 1951.

(7) Chute, R., and Soutter, L.: Thoraco-abdominal nephrectomy for large kidney tumors. J. Urol. 61: 688-696, Apr. 1949.

(8) Chute, R.; Soutter, L.; and Kerr, W. S., Jr.: Value of thoracoabdominal incision in removal of kidney tumors. New England J. Med. 241: 951-960, Dec. 15, 1949.

(9) Chute, R.: Thoraco-abdominal incision in urological surgery. J. Urol. 65: 784-794, May 1951.

(10) Sweet, R. H.: Thoracic Surgery. W. B. Saunders Co., Philadelphia, Pa., 1950. p. 213.

on the left. The flank and paravertebral incisions, even with resection of the twelfth or eleventh ribs, provide a limited exposure. Definitive surgery by means of these approaches is fraught with danger because the exposure is inadequate for accurate control of the adrenal blood supply. Poor exposure is particularly dangerous in patients with pheochromocytoma in whom digital manipulation of the tumor in order to deliver it may result in a fatal paroxysm of hypertension.

Exposure of the adrenal area, by entering the pleural space through the ninth or tenth interspace and incising the diaphragm, obviates these difficulties and permits a safe, orderly resection of whatever lesion may be present. The degree of exposure is superlative and cannot be equaled by any other approach. Rib resection or fracture has been unnecessary in either case. Transthoracic or thoracoabdominal approaches for upper abdominal operations may be accomplished without increased morbidity or mortality over that of abdominal, flank, or lumbar incisions.

CASE REPORTS

Case 1. A 49-year-old man was transferred to this hospital on 27 December 1951 because of hemoptysis occurring 1 week previously. He had been discharged from the military service in 1945 with a diagnosis of hypertensive vascular disease and had been under the care of a private physician who had treated him with diet, phenobarbital, and restriction of activity. Aside from the episode of hemoptysis his only symptoms were severe intermittent headaches and slight dyspnea. The headaches occurred from 1 to 3 times daily, were sudden in onset, and lasted for from a few minutes to 3 hours. The systolic blood pressure had been recorded as high as 240. The physical findings, except for the blood pressure, were within normal limits.

Because of the intermittent character of the headaches, the blood pressure was taken every 30 minutes. The resultant chart revealed that the patient maintained levels of about 130/80 most of the time and that corresponding to the onset of an attack of headache the blood pressure would rise abruptly, reaching levels as high as 275/120. Seventeen milligrams of piperoxane hydrochloride given intravenously during a hypertensive seizure resulted in a precipitous drop in systolic pressure from 265 to 210 over an 11-minute period.

Serial ECG's were interpreted as showing myocardial ischemia. Roentgenograms following retroperitoneal oxygen insufflation clearly demonstrated a 4- by 4-cm. rounded shadow in the right adrenal area.

On 25 February 1952 the right adrenal area was explored through a thoracoabdominal incision. A firm tumor mass measuring 4 by 4 cm. was discovered lying in the medullary portion of the gland. The tumor was resected without difficulty. The postoperative course was uneventful. The patient's blood pressure remained at normal levels and there was no recurrence of headaches. The pathologist reported a benign pheochromocytoma.

Case 2. A 31-year-old woman was transferred to this hospital on 2 February 1952 with a tentative diagnosis of Cushing's syndrome. Her illness began in 1945 when she developed increasing obesity, swelling of the lower extremities, and fatigability. During the interval from the onset until 6 weeks prior to admission she developed, with intermittent regression and progression, hirsutism, deepened vocal tone, amenorrhea, abdominal strias, rounded facies, and hypertension. In August 1951 she was successfully delivered at term of a live infant following a pregnancy which was complicated by severe hypertension. Six weeks prior to admission she developed progressive signs of cardiac failure characterized by peripheral edema, dyspnea, hemoptysis, and oliguria.

Physical examination revealed the external characteristics of Cushing's syndrome, a blood pressure of 200/120, dependent edema, and evidence of pulmonary edema. Urinalysis showed persistent albuminuria (200 mg. per 100 cc.). The serum cholesterol was 556 mg. per 100 cc. The glucose tolerance was impaired. Urinary 17-ketosteroids ranged from 15.2 to 64.5 mg. per 24 hr. Following an intravenous injection of phenolsulfonphthalein there was 5 percent excretion in 15 min. The ECG showed left axis deviation. Roentgenograms of the chest revealed moderate cardiac enlargement, predominately left ventricular. A gallbladder series showed a functioning gallbladder with cholelithiasis. Roentgenograms following retroperitoneal oxygen insufflation revealed a 45-by 60-mm. oval tumor mass lying in the area of the right adrenal gland.

The patient was treated by digitalization, diuretics, salt-poor diet, and bed rest with some improvement and weight loss. After giving 100 mg. of cortisone daily for 3 days preoperatively, she was taken to surgery on 21 March. A thoracoabdominal incision was made. As soon as the diaphragm was opened the tumor was visualized and resection was accomplished without incident. The left adrenal gland was palpated and believed to be normal. The postoperative course was uneventful. The dosage of cortisone was gradually decreased and after 10 days discontinued. ACTH was administered in diminishing doses starting

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with 25 mg., and discontinued after 10 days. The patient subsequently manifested no symptoms of adrenal insufficiency. The pathologist reported a benign adrenocortical adenoma.

Case 3. A 45-year-old man was admitted to the hospital on 16 April 1952 complaining of headache, nausea, and vomiting. He stated that the headaches first began in 1949. The onset of each headache was rapid, occurring usually in the midmorning and lasting for from 30 minutes to 2 hours, then slowly subsiding. His pain was bilateral and was located in the frontal and temporal areas. Frequently nausea would accompany the attack. He had been admitted previously for the same complaints. During the investigation at that time he had a histamine gastric analysis. The injection of histamine precipitated a severe attack of headache associated with syncope. He was discharged with a neuropsychiatric diagnosis.

Examination, except for the blood pressure, was within normal limits. The blood pressure taken during one of the attacks was recorded as high as 290/196. In the interim between attacks his blood pressure was recorded at about 130/90. Eighteen milligrams of piperoxane hydrochloride, given during a paroxysm of hypertension, resulted in a precipitous drop in his blood pressure from 290/196 to 165/118 within 20 minutes. Roentgenograms following retroperitoneal oxygen insufflation revealed that there was a 6- by 6-cm. rounded tumor mass lying in his right adrenal area.

On 9 May he was taken to surgery. A transthoracic approach was made. The tumor was easily palpable as soon as the diaphragm was opened and resection was accomplished without incident. As soon as the tumor was removed his blood pressure dropped to unobtainable levels despite the rapid administration of norepinephrine. At this time he developed ventricular tachycardia and within 1 minute cardiac arrest occurred. The pericardium was opened and his heart was found to be in standstill. Massage was begun and 0.5 cc. of 1:1000 epinephrine was injected into his heart. Massage was continued and another injection of epinephrine was given 5 minutes later. At this time his heart began to beat regularly at a rate of 40 to 50 beats per minute. An ECG revealed that a ventricular rhythm was present. His blood pressure was recorded during this time at about 70/40. After 1½ hours, P waves began to appear in the ECG and a normal sinus rhythm was soon re-established. It was necessary to give norepinephrine intravenously to maintain his blood pressure in the next 24 hours, but after that his recovery was uneventful. His blood pressure remained at normal levels and there was no recurrence of headaches. There was no evidence of damage to the central nervous system from the period of cardiac arrest.

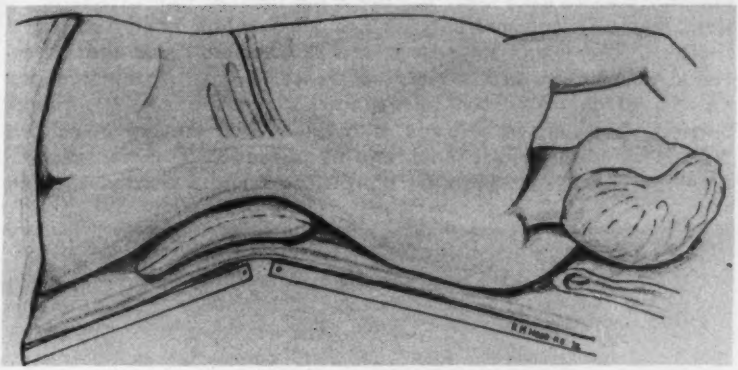

Figure 1. A drawing showing the position of the patient on the operating table and the approximate location of the incision.

OPERATIVE TECHNIC

Anesthesia is induced with an intravenous injection of pentothal sodium and an endotracheal tube introduced. Anesthesia is then changed to ether-oxygen for the remainder of the procedure. The patient is placed in the position shown in figure 1. A skin incision from 10 to 12 inches long is made over the ninth or tenth interspace, beginning about 1 inch from the spinous processes and extending to the end of the interspace and as far

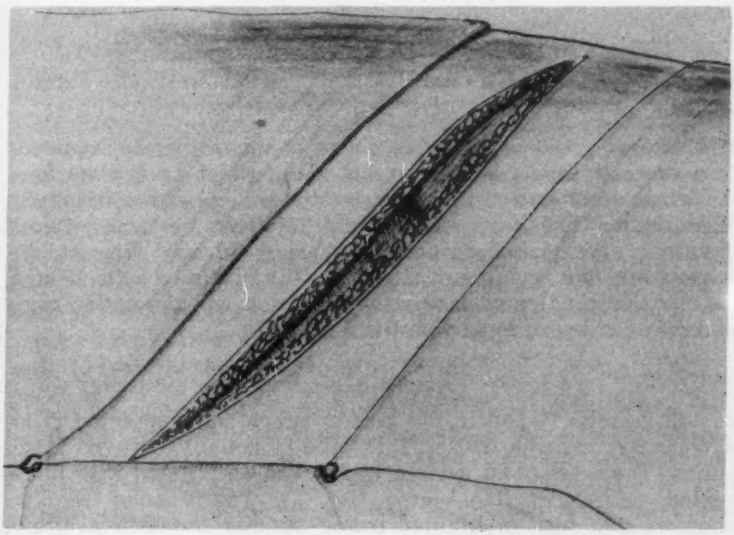

Figure 2. A drawing showing the completed skin incision.

anteriorly as is necessary to obtain the desired exposure (fig. 2). Hemostasis is accomplished with electrocautery or by individual ligature. The latissimus dorsi, the external oblique, and the internal oblique are incised and separated (fig. 3). The intercostal muscle of the selected interspace is incised and the pleura opened. The lung is allowed to collapse and the chest wall retracted by means of a Finochietto rib spreader. The diaphragm is then incised in the direction of its fibers and retracted (fig. 4).

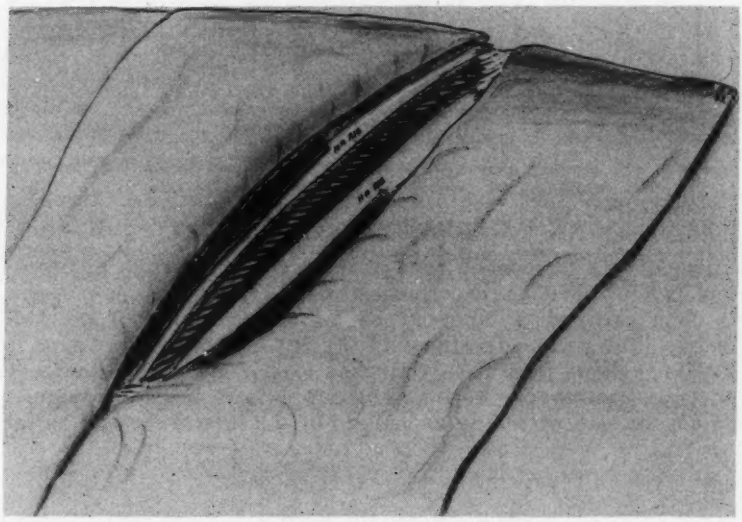

Figure 3. A drawing showing the incision after the latissimus dorsi had been divided, thereby exposing the tenth interspace.

The adrenal gland imbedded in perirenal fat is thereby exposed. The vascular supply of the adrenal gland which is derived from the aorta, renal artery, and phrenic artery is isolated under direct visualization and complete control. This can be done without disturbing the gland appreciably. The gland may then be delivered into the wound and resected. The opposite adrenal area can be easily palpated through the incision and the entire upper abdomen can be explored with little difficulty.

The diaphragm is repaired with interrupted sutures of fine cotton. The subdiaphragmatic space is not drained, but an intercostal catheter is left in the pleural space and connected to an underwater drainage bottle. This tube is usually removed in 24 hours. The intercostal muscle and pleura are closed with interrupted sutures of fine cotton (fig. 5). The muscles are reapproximated with interrupted cotton sutures and skin and subcutaneous tissues are closed with interrupted vertical mattress sutures of fine cotton.

DISCUSSION

Although we have used the thoracoabdominal incision in 2 of the 3 cases, it is considered that the abdominal extension has been largely unnecessary. In case 3 the incision was not extended beyond the costal arch and it was found that the exposure was satisfactory. In future patients it is intended that the incision will not include an abdominal extension. Grimson et al. *(5)*

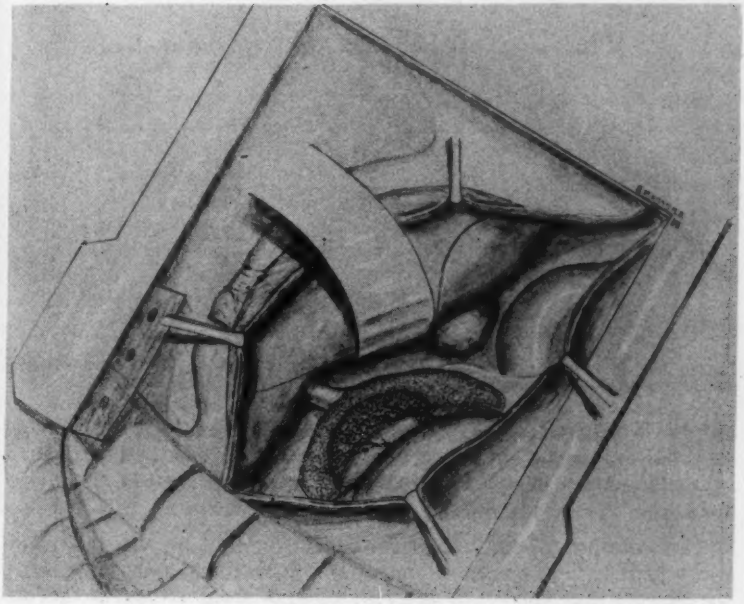

Figure 4. A drawing showing the exposure of the pheochromocytoma in patient 1. Note the wide exposure obtained without manual retraction, leaving the adrenal gland and its tumor in a position for operation under direct vision.

have indicated the importance of not entering the peritoneal cavity, but we believe that this may be done without compunction and, in fact, is necessary if the opposite adrenal area or the upper abdomen is to be explored.

Repeated notations are found in the literature as to the necessity for exposing both adrenal glands at the same time, even if 2 operations are necessary. By using the retroperitoneal, oxygen-insufflation technic *(11)* we have been able positively to demonstrate the tumor mass in each case. If diffuse adrenal hyperplasia is the primary disease, a definite tumor mass will

(11) Steinbach, H. L.; Lyon, R. P.; Miller, E. R.; and Smith, D. R.: Extraperitoneal pneumography; preliminary report. California Med. 75: 202-207, Sept. 1951.

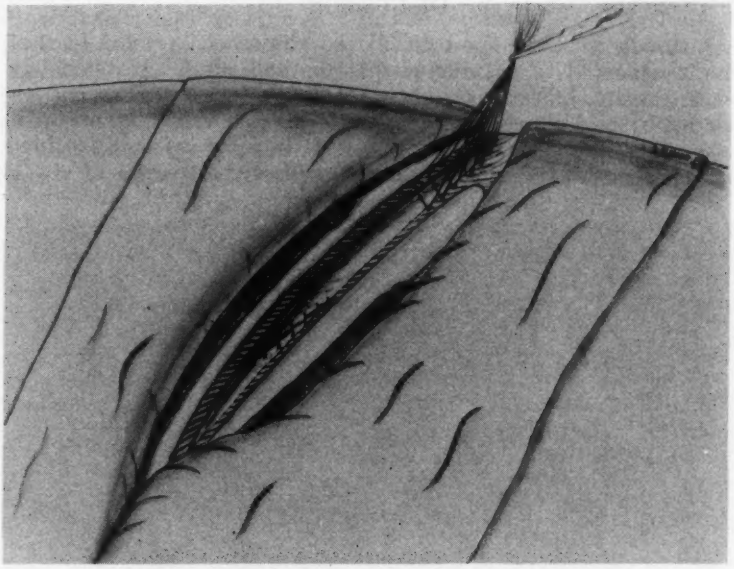

Figure 5. A drawing showing the wound after repair of the diaphragm and closure of the intercostal space by interrupted sutures.

not be differentiated, but discrepancy in the size of the glands may be apparent. Therefore, we believe that bilateral exposure is unnecessary in most patients and certainly not at the same time.

The retroperitoneal, oxygen-insufflation technic via the retrorectal space represents an important forward step in the ability to demonstrate tumors in the renoadrenal area. It can be accomplished safely and painlessly by the unexperienced operator with consistently good results. This technic should not be confused with the older technic of perirenal insufflation which was associated with a high mortality rate. In most cases the patient experienced excruciating pain and the resulting roentgenographic studies were inconsistent or useless.

EXPERIMENTAL LOCATION OF MYOCARDIAL INFARCTION USING RADIOISOTOPES[1]

WALTER K. YATES, *Captain, U. S. A. F. (MC)*

ACCURATE determination of the location and size of a myocardial infarction has long been a problem at postmortem examination. Infarctions are often difficult to find by either gross or microscopic methods. This situation constitutes a dilemma for the pathologist, the clinician, and the student of electrocardiography. This report describes a simple method, based on the absence of a radioactive isotope in the infarcted area, whereby an accurate determination of the size and position of the infarction may be made at autopsy.

PROCEDURE

The method was developed and demonstrated on 13 dogs in which experimental infarctions were induced by the following procedure. The extremities were shaved to allow proper contact of electrocardiographic electrodes. The anterior surface of the chest was shaved and surgically prepared. The animal was anesthetized with an intravenous injection of pentobarbital sodium and an oxygen cannula was inserted into the trachea. Cannulas were inserted into the femoral artery for direct blood pressure determinations and into the femoral vein for fluid administration. ECG's were recorded, using the standard limb leads, the unipolar limb leads, and leads V_1, V_2, V_4, and V_5. The chest was then opened at the left sternal border and the pericardium was separated. The desired coronary artery was identified and ligated. Prior to its ligation, procaine amide hydrochloride was administered intravenously to prevent ventricular fibrillation. Following ligation of the coronary artery, frequent ECG's were taken to detect the presence of developing myocardial infarction. Following appearance of a tracing typical of infarction, a radioisotope was injected intravenously. In this series radiophosphorus (P–32) was used. The amount of P–32 varied, but was usually of the order of 0.5 millicurie. At an arbitrary interval after injection of P–32, the animal was sacrificed and the heart removed for autoradiography.

(1) Experimental study conducted by the author while attending the Atomic Warfare Program at The Oak Ridge Institute of Nuclear Studies.

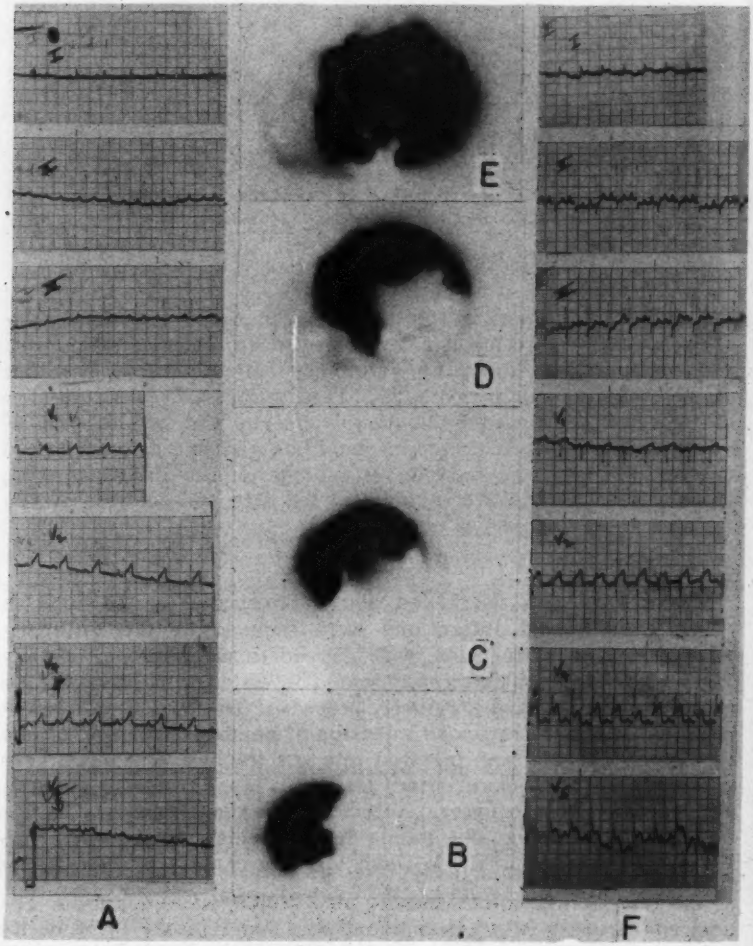

Figure 1. Experiment 5. Autoradiogram taken with anterior surface of cardiac slices downward. (A) *Control ECG.* (B) *Apex.* (C) *and* (D) *Intermediate.* (E) *Base.* (F) *ECG after occlusion.*

The technic of autoradiography has been discussed at length *(2-4)* and will not be reviewed here except to note the application of the technic to this experiment.

(2) Boyd, G. A.: The Physical Principles and Techniques of Autoradiographs. MDDC-1226. U. S. A. E. C., Oak Ridge, Tenn.

(3) Axelrod, D. J.: The Radioautographic Technique. Circular A-4. Isotopes Division, U. S. A. E. C., Oak Ridge, Tenn.

(4) Evans, T. C.: Radioautographs in which tissue is mounted directly on photographic plate. Proc. Soc. Exper. Biol. & Med. 64: 313-315, Mar. 1947.

The heart was cut into serial transverse sections from base to apex. These sections were frozen, placed on roentgenographic film, and stored in a freezing unit during exposure. The circulation of the blood through nonoccluded arteries deposited the isotope uniformly in the normal myocardium. Because of the decreased circulation of the infarcted area, it was not supplied with

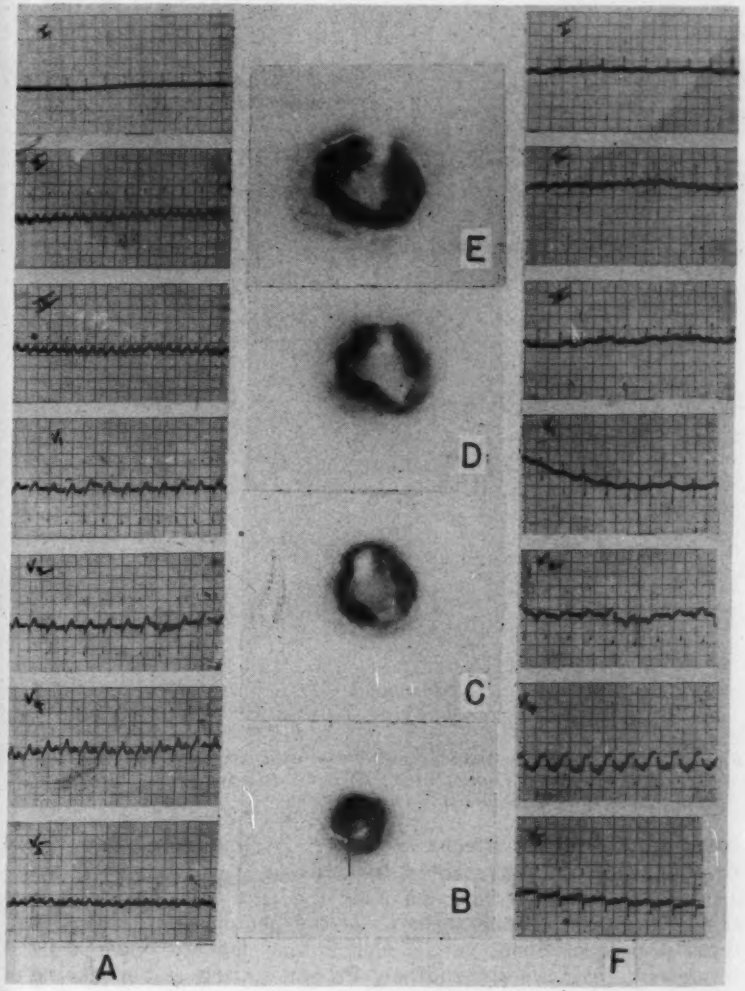

Figure 2. Experiment 7. Autoradiogram taken with anterior surface of cardiac slices downward. (A) *Control ECG.* (B) *Apex.* (C) *and* (D) *Intermediate.* (E) *Base.* (F) *ECG after occlusion.*

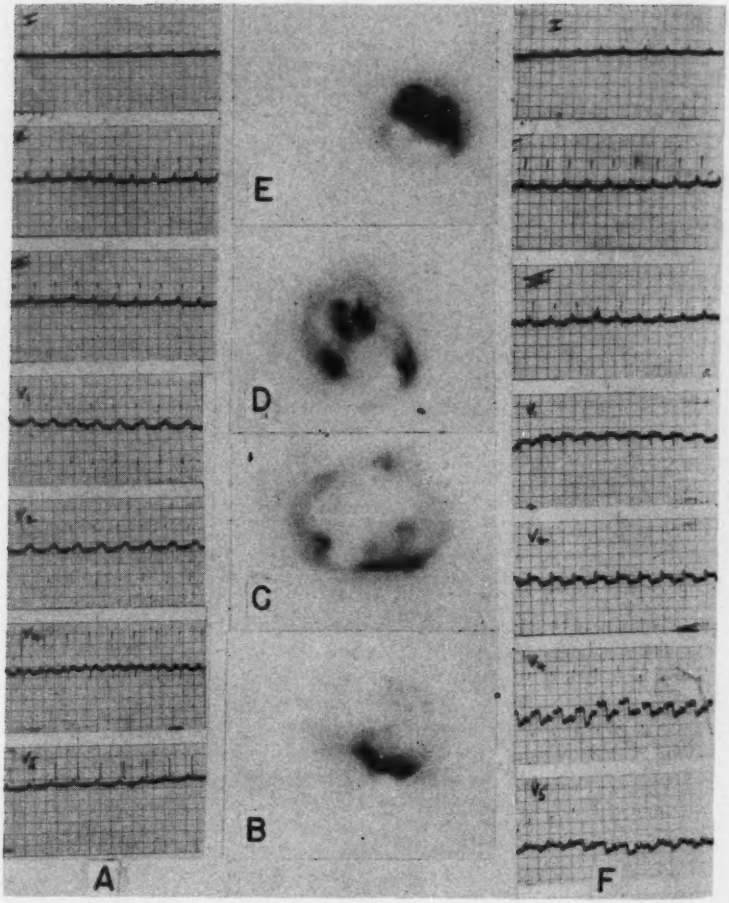

Figure 3. Experiment 9. Autoradiogram taken with anterior surface of cardiac slices downward. (A) *Control ECG.* (B) *Base.* (C) *and* (D) *Intermediate.* (E) *Apex.* (F) *ECG after occlusion.*

isotope and hence was not radioactive. Radioactive tissue placed in apposition to photographic film causes a latent image in the emulsion which can be seen after the film is developed. Inert tissue causes no latent image. On the photographic negative of these tissue sections, normal myocardium appears black and the infarcted areas are transparent. Proper cutting and arranging of these serial sections produces a three-dimensional conception of the exact size and position of the infarction. Representative examples of this technic are presented, including the control ECG, autoradiogram, and ECG after occlusion.

RESULTS

Experiment 5. The left coronary artery was ligated near its source, causing an anterolateral myocardial infarction. The control ECG and a tracing taken 35 minutes after occlusion are shown in figure 1. One millicurie of P–32 was injected intravenously following this tracing and 45 minutes later the animal was sacrificed. The autoradiogram portrays transverse sections of the

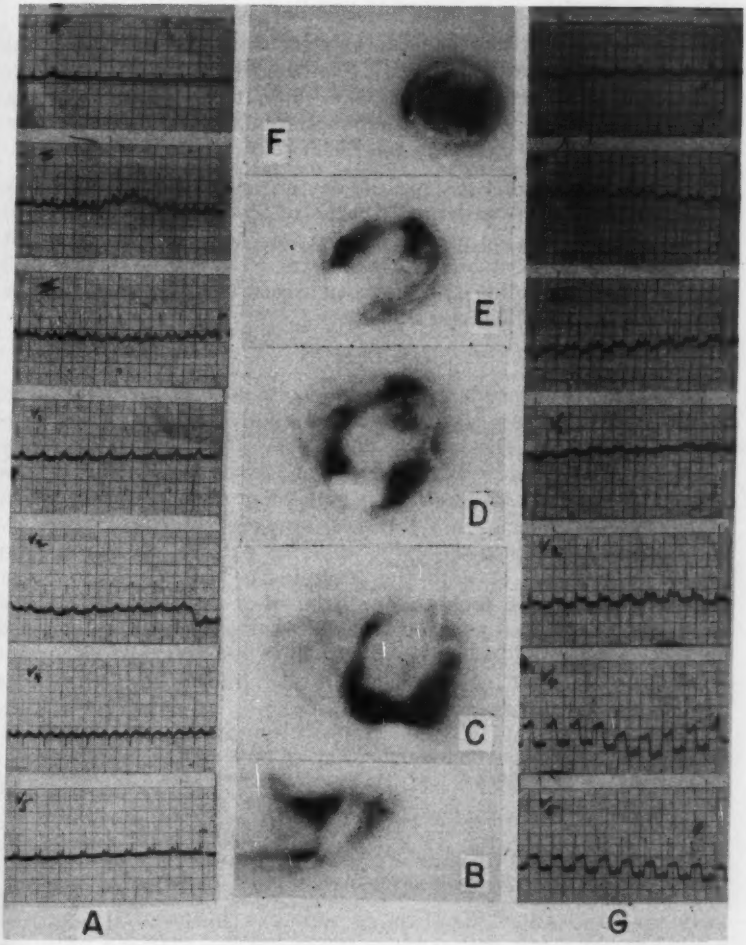

Figure 4. Experiment 10. Autoradiogram taken with anterior surface of cardiac slices downward. (A) *Control ECG.* (B) *Base.* (C), (D), *and* (E) *Intermediate.* (F) *Apex.* (G) *ECG after occlusion.*

heart. The ECG shows an anterolateral infarction. This is corroborated by the radiographic "hole" in the anterolateral surface of the left ventricle.

Experiment 7. The chest was opened and the right coronary artery was ligated on the posterior surface of the heart. The ECG shows the control and a tracing taken 90 minutes after occlusion (fig. 2). Five-tenths millicurie of P–32 was used in this experiment. As indicated by the definite radiographic "hole" in that area, the infarction is posterior in position.

Experiment 9. In this case an anterior occlusion was produced near the base of the heart and 0.5 millicurie of P–32 was used. The control ECG and a tracing taken 30 minutes after occlusion are shown in figure 3. An anteroseptal infarction is evident in both the autoradiogram and in the ECG.

Experiment 10. In this experiment an anterior occlusion was accomplished. Four-tenths millicurie of P–32 was injected 50 minutes after occlusion and the animal was sacrificed 2 hours and 20 minutes after occlusion. The control ECG and that taken 40 minutes after occlusion are shown in figure 4. The autoradiogram and the ECG reveal anterior infarction.

DISCUSSION

An objective procedure is more accurate than conventional technics for the postmortem location and visualization of myocardial infarction. The method described is of interest primarily to students of electrocardiography and is most applicable to experimental animals. It might be modified in such a manner as to have clinical applications. For example, electronic radiation detection may develop to the point where an external Geiger counter would be capable of detecting radiologic "holes" in vivo. In such an event, this technic would be of great value in clinical diagnosis. It is also possible that this method could be adapted for use in patients in extremis who have obscure electrocardiographic findings. This would add to the information obtained at postmortem examination.

LIVER BIOPSY IN MALARIA[1]

ROBERT C. HUNTER, Jr., *Lieutenant Colonel, MC, U. S. A.*
JOHN A. SHEEDY, *Major, MC, U. S. A.*

THE presence of jaundice in patients with malaria has been noted frequently *(2-6)* although the incidence varied widely (table 1). Stratman-Thomas *(7)* stated that this jaundice was caused by rapid destruction of red blood cells which also produced a marked anemia. Radvan and Apreotesci *(8)* pointed out that hemolysis did not always account for the jaundice because icterus was present in some patients without detectable anemia. Other authors have indicated that hepatocellular damage (manifested by hepatomegaly *(3, 6, 9)*; elevated cephalin-cholesterol flocculation *(6, 9-15)*; decreased serum albumin

(1) Letterman Army Hospital, San Francisco, Calif.

(2) Hills, A. G.: Malarial jaundice. Am. J. M. Sc. 212: 45-53, July 1946.

(3) Kern, R. A., and Norris, R. F.: Liver involvement in malaria. U. S. Nav. M. Bull. 43: 847-858, Nov. 1944.

(4) Bunker, H. A., Jr., and Kirby, G. H.: Treatment of general paralysis by inoculation with malaria. J. A. M. A. 84: 563-568, Feb. 21, 1925.

(5) Chalmers, T. C., Jr.: Occurrence of jaundice in therapeutic and natural malaria. J. Clin. Investigation 26: 1055-1059, Nov. 1947.

(6) Read, H. S.; Kaplan, L. I.; Becker, F. T.; and Boyd, M. F.: Analysis of complications encountered during therapeutic malaria. Ann. Int. Med. 24: 444-464, Mar. 1946.

(7) Stratman-Thomas, W. K.: Infection in intermediate host symptomatology; vivax malaria. In American Association for the Advancement of Science (M. F. Boyd, Chairman, Publication Committee): A Symposium on Human Malaria With Special Reference to North America and the Caribbean Region. Publication No. 15. American Association for the Advancement of Science, Washington, D. C., 1941. pp. 183-189.

(8) Radvan, I., and Apreotesci, C.: La bilirubinémie paludéenne par rapport à la physiopathologie et à la thérapeutique. Riv. di malariol. 26: 183-190, Aug. 1947.

(9) Fredricks, M. G., and Hoffbauer, F. W.: Study of hepatic function in therapeutic malaria. J. A. M. A. 128: 495-499, June 16, 1945.

(10) Lippincott, S. W.; Ellerbrook, L. D.; Hesselbrock, W. B.; Gordon, H. H.; Gottlieb, L.; and Marble, A.: Liver function tests in chronic relapsing vivax malaria. J. Clin. Investigation 24: 616-622, Sept. 1945.

(11) Schneider, J. (Paris), and Hartman, L.: Explorations fonctionnelles hépatiques au cours du paludisme, Étude systématique au cours du paludisme d'inoculation. Bull. Soc. path. exot. 42: 259-267, Jan. 1949.

(12) Makari, J. G.: Cephalin flocculation test in malaria. Brit. M. J. 1: 272-273, Feb. 23, 1946.

(13) Guttman, S. A.; Potter, H. R.; Hangar, F. M.; Moore, D. B.; Pierson, P. S.; and Moore, D. H.: Significance of cephalin-cholesterol flocculation test in malarial fever. J. Clin. Investigation 24: 296-300, May 1945.

(14) Kopp, I., and Solomon, H. C.: Liver function in therapeutic malaria. Am. J. M. Sc. 205: 90-97, Jan. 1943.

(15) Mirsky, I. A.; von Brecht, R.; and Williams, L. D.: Hepatic dysfunction in malaria. Science 99: 20-21, Jan. 7, 1944.

(11, 13, 16); reduced serum cholesterol and cholesterol esters *(11, 13, 14)*; and increased bromsulphalein retention, particularly in the jaundiced patients *(2, 3, 5, 9, 13, 14))* was a factor in producing this jaundice.

TABLE 1. *Incidence of jaundice in malaria*

Authors	Type of malaria	Number of patients	Percent with jaundice
Hills *(2)*	Natural	8,837	0.27
Kern and Norris *(3)*	Natural	54	61.0
Bunker and Kirby *(4)*	Therapeutic	53	34.0
Chalmers *(5)*	Therapeutic	450	8.0*
Read et al. *(6)*	Therapeutic	300	7.3

*Some of these patients were thought to have impaired hepatic function before they were given malaria.

Manson-Bahr *(17)* described extensive damage in the livers of patients dying of malaria, the degree of damage varying with the intensity of the infection. The livers were enlarged and pigmented. The parenchymal cells showed all stages of destruction, with cloudy swelling and, in severe cases, widespread central necrosis. These cells contained hemosiderin and gave the Prussian blue reaction. The sinusoids were congested and contained malarial parasites. The Kupffer cells contained the malarial pigment, hemozoin, which did not give the Prussian blue reaction unless pretreated with nitric acid and hydrogen peroxide.

These pathologic changes were found in patients dying of severe malaria and in whom fever, toxicity, and anemia may have combined to produce liver damage of a nonspecific nature. There has been a paucity of information on the histology of the liver in nonfatal cases of malaria. Fredericks and Hoffbauer *(9)* reported a biopsy of a normal-appearing liver in a patient with malaria. Milanes et al. *(18)* also reported a patient with malaria in whom liver biopsy showed degeneration of the polygonal cells, periportal round-cell infiltration, and pigment in the Kupffer cells, but, as the authors stated, concomitant viral hepatitis could not be ruled out.

(16) Kopp, I., and Solomon, H. C.: Relationship of hypoalbuminemia to edema of malaria. Am. J. M. Sc. 202: 861-868, Dec. 1941.

(17) Manson-Bahr, P. H.: Manson's Tropical Diseases. 12th edition. Williams & Wilkins Co., Baltimore, Md., 1945.

(18) Milanes, F.; Leon Blanco, P.; Llanio, R.; and Causa, A.: Sobre un caso de paludismo con ictero hepatocelular. ¿ Secundario o concomitante? Consideraciones patogénicas. Vida nueva 63: 41-49, Feb. 1949.

In experimental malaria in animals, Andrews *(19)* demonstrated centrilobular degeneration and necrosis as well as fatty infiltration in the liver. The sinusoids were congested with parasitized erythrocytes and the Kupffer cells were swollen with red blood cells, pigment, parasites, and debris. He attributed the parenchymal-cell damage to anoxia.

The present study was undertaken in an effort to elucidate the nature of jaundice occurring in malarial patients, with particular reference to the histologic changes in the liver as shown by needle biopsy specimens. It is based on 8 selected patients with malaria, caused by *Plasmodium vivax* in 7 and type undetermined in 1. The clinical findings were similar to those of viral hepatitis in all 8 patients. Twenty unselected patients with viral hepatitis seen during the same period served as controls.

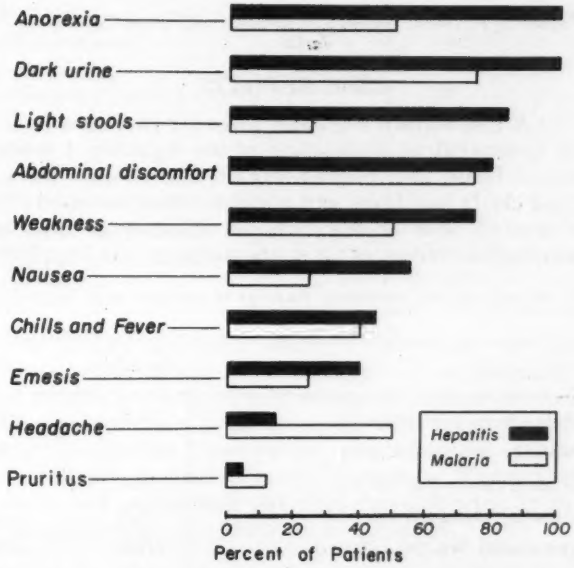

Figure 1. Symptoms in patients with hepatitis and malaria.

RESULTS

The symptoms (fig. 1) and physical findings (fig. 2) in the group of 8 patients with malaria were similar to those in the group of 20 with viral hepatitis. The initial laboratory findings (table 2) also showed more similarities than differences. Additional miscellaneous comparisons (table 3) showed that the

(19) Andrews, W. H. H.: Liver lesions in malaria. Tr. Roy. Soc. Trop. Med. & Hyg. 41: 699-702, May 1948.

duration of the illness was distinctly less in the patients with malaria. One-half of the patients with hepatitis were diagnosed serum hepatitis, the other half, infectious hepatitis. There was no history of excessive use of alcohol or exposure to hepatotoxic agents in either group. All of the patients recovered.

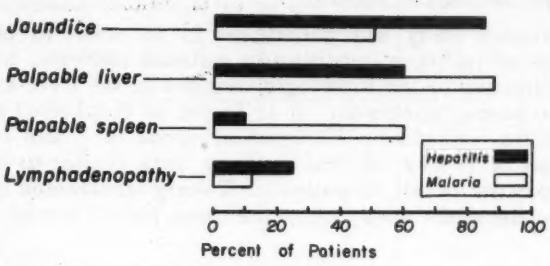

Figure 2. Physical findings in patients with hepatitis and malaria.

CASE REPORTS

Case 1. A 22-year-old man was wounded in Korea on 1 March 1951 and underwent an amputation of the right leg 1 week later. He received blood and plasma during this period. On 4 and 6 May he had chills and fever and a blood smear revealed *P. vivax*. He was treated with chloroquine. On 20 July he was given a blood transfusion during another operation on his leg. His hemo-

TABLE 2. *Average initial laboratory findings in patients with hepatitis and malaria.*

	Hepatitis	Malaria
Hemoglobin (grams per 100 cc.)	14.2	12.6*
Serum bilirubin (mg. per 100 cc.)	7.8	3.0
Serum albumin (grams per 100 cc.)	4.4	3.6
Serum globulin (grams per 100 cc.)	3.3	3.5
Serum cholesterol (mg. per 100 cc.)	226.0	140.6
Serum cholesterol esters (percent of cholesterol)	52.2	62.2
Urine urobilinogen (Ehrlich units per 2 hours)	2.1	2.4
Zinc sulfate turbidity	18.0	16.2
Thymol turbidity	13.7	12.7
Cephalin-cholesterol flocculation**	11	7

*Includes 2 patients with severe hemolysis and hemoglobin of 6.1 and 10.7 gm. respectively.

**This figure is *not* an average but the actual number of patients with readings greater than 2 plus.

globin was 13.3 following the operation. On 18 August he lost his appetite and several days later his urine became dark and his skin jaundiced. His serum bilirubin was 4.5 mg. per 100 cc.; thymol turbidity, 12; cephalin-cholesterol flocculation, 3 plus; blood cholesterol and proteins, normal. During the next 3 weeks his jaundice gradually deepened and on 14 September he was transferred to the medical service with a serum bilirubin of 14.9 mg. per 100 cc. On 17 and 19 September he again had chills and fever and a blood smear again revealed *P. vivax*. He was treated with chloroquine and had no further recurrences of malaria. By November he had completely recovered from the hepatitis.

TABLE 3. *Miscellaneous comparative findings in patients with hepatitis and malaria*

	Hepatitis	Malaria
Average age (years)	24.9	24.4
Number of patients who had had a transfusion or venipuncture within 6 months	10	2
Number of patients who had had a gradual onset	13	6
Number of patients who had had an acute onset	7	6
Delay prior to hospitalization (days)	8.7	5.5
Duration of clinically evident hepatocellular disease (weeks)	9.2	4.3

A liver biopsy specimen taken 2 days after his last chill showed the parenchymal cells arranged in an irregular pattern, granular cytoplasm, and a small amount of pigment in some cells. Occasional nuclei were hyperchromatic with an increased nuclear-cytoplasmic ratio and other nuclei were multiple. In places, the small bile ducts contained inspissated bile. There were a few round cells and occasional polymorphonucleocytes in the portal areas. The pathologic diagnosis was hepatitis.

Case 2. A 23-year-old man noted the gradual onset of anorexia on the day after his return to the United States from Korea. This was followed during the next 2 weeks by nausea, vomiting, fever, dark urine, light stools, and jaundice. The only significant physical finding was jaundice. His hemoglobin was 17.8; serum bilirubin, 9.4 mg. per 100 cc.; thymol turbidity, 16; cephalin-cholesterol flocculation, 4 plus; serum albumin, 3.5 grams per 100 cc.; and serum globulin, 3.8 grams per 100 cc. On the twentieth hospital day he had a chill, a temperature of 103° F., and headache. Blood smear revealed *P. vivax*. His malaria responded

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promptly to chloroquine and did not recur. His hepatitis subsided slowly but completely.

A liver biopsy specimen taken 1 week after the chill showed the liver architecture to be well preserved. There was a slight increase in the size and cellularity of the portal areas, the cells being nearly all lymphocytes. In some areas this infiltration extended into the peripheral portion of the lobules. There was some evidence of active degeneration of the parenchymal cells, as well as moderate nuclear variation suggesting regeneration. The pathologic diagnosis was hepatitis.

Case 3. A 19-year-old man noted anorexia, nausea, vomiting, upper abdominal pain, chills, fever, headache, and dark urine on board ship returning to the United States from Japan. One week later he was admitted to sick bay, appearing pale, lethargic, slightly jaundiced, and with a temperature of 102.2° F. A blood smear for malaria was negative. He arrived at this hospital a week later still pale, lethargic, with a lemon-yellow icterus, a palpable liver and spleen, a slight generalized lymphadenopathy, and a normal temperature. Blood smear again failed to show malarial parasites. His hemoglobin was 6.1; serum bilirubin, 1.2 mg. per 100 cc., with a rise to 2.3 the next week; thymol turbidity, 10; cephalin-cholesterol flocculation, 4 plus; serum cholesterol, 101 mg. per 100 cc.; cholesterol esters, 68 mg. per 100 cc.; serum albumin, 2.8 grams per 100 cc.; and serum globulin, 2.4 grams per 100 cc. He had mild temperature elevations of from 99 to 100° F. during the first 7 days of hospitalization. Sternal marrow examination then revealed *P. vivax*. Treatment with chloroquine was started on the eighth hospital day. His temperature rose to 102° F. on the following day, then returned to normal. All of his symptoms cleared rapidly and his anemia gradually disappeared. Two months later he had a chill and fever and a peripheral blood smear revealed *P. vivax*. On the day following the chill his urine urobilinogen was 13.5 Ehrlich units per 2 hours; serum bilirubin, 2.7 mg. per 100 cc.; thymol turbidity, 8; and cephalin-cholesterol flocculation, 3 plus. His hemoglobin was not checked until 1 week later when it was 15.1. He was treated with chloroquine and quinine with a rapid resolution of symptoms and findings. A liver biopsy specimen taken 2 days after the last chill revealed a normal liver.

Case 4. A 40-year-old man gave a history of several episodes of chills and fever during a 9-month tour in Korea. No diagnosis was made and no treatment was given. About 3 weeks after his return to the United States he noted fever, headache, muscular aches, nightly chills, and sweats. By the time of his admission to this hospital 10 days later he was complaining also of easy

fatigability, shortness of breath, dark urine, and mental confusion. Examination revealed a pale, lethargic patient with a palpable spleen, moderate pitting edema of the ankles, and no fever. His hemoglobin on admission was 10.7, dropping to 7.3 five days later. A blood smear revealed *P. vivax*. His serum bilirubin was 4.4 mg. per 100 cc.; thymol turbidity, 11; cephalin-cholesterol flocculation, 4 plus; prothrombin activity, 46 percent; serum cholesterol, 78 mg. per 100 cc.; serum albumin, 2.1 grams per 100 cc.; and serum globulin, 2.9 grams per 100 cc. He had a daily chill and a temperature rise to 102 or 103° F. for 3 days following admission. Chloroquine therapy was started on the second hospital day, and his symptoms cleared rapidly, although blood smears continued to show *P. vivax* until the fifteenth hospital day.

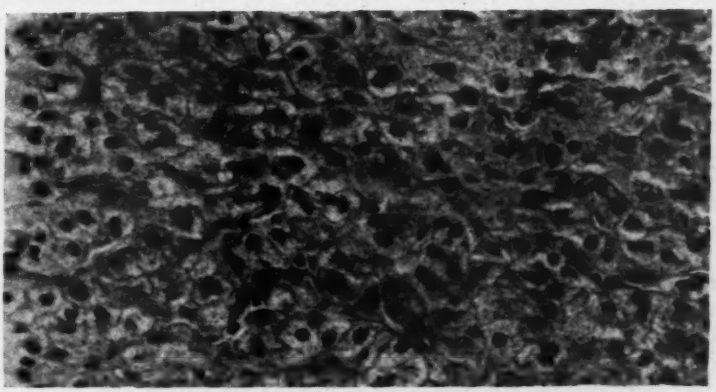

Figure 3. Section of liver. Note the fine granular pigment in the Kupffer cells.

A liver biopsy specimen was obtained on the sixteenth hospital day. The tissue appeared normal with the exception of some nuclear variation in the parenchymal cells and a granular, dark brown pigment in the Kupffer cells (fig. 3). The findings were considered consistent with hemolysis.

Case 5. A 19-year-old man noted anorexia and malaise with a shaking chill, fever, and headache on the day after his return to the United States from Korea. He was admitted to this hospital where examination revealed a palpable liver and spleen and a temperature of 98° F. His hemoglobin was 13.3; serum bilirubin, 2.1 mg. per 100 cc.; thymol turbidity, 13; cephalin-cholesterol flocculation, 3 plus; prothrombin activity, 59 percent; serum cholesterol, 99 mg. per 100 cc.; cholesterol esters, 63 mg. per 100 cc.; serum albumin, 3.8 grams per 100 cc.; and serum globulin, 4 grams per 100 cc. Blood smear was positive for *P. vivax*.

On the evening of admission and again the next morning, he had a chill with a temperature rise to 103.6° F. He was treated with chloroquine and had a rapid and complete recovery. A liver biopsy specimen taken 6 days after his last chill revealed a normal liver.

Case 6. A 20-year-old man had an episode of headache, chills, and fever on board ship when returning from Korea. Six days later he had a recurrence, but on this occasion he also had dark urine. He was admitted to the sick bay. Blood smears failed to reveal malarial parasites. On arrival at this hospital 1 week later, he appeared acutely ill, was slightly jaundiced, had a palpable liver and spleen, and no fever. A blood smear was positive for *P. vivax*. His hemoglobin was 12.7; serum bilirubin, 1.3 mg. per 100 cc.; thymol turbidity, 16; cephalin-cholesterol flocculation, 4 plus; serum cholesterol, 49 mg. per 100 cc.; cholesterol esters, 5 mg. per 100 cc.; serum albumin, 3 grams per 100 cc.; and serum globulin, 3.5 grams per 100 cc. Three days after admission he had a chill and his temperature rose to 104.6° F. Chloroquine therapy was started on the same day and his symptoms and findings cleared rapidly. A liver biopsy specimen obtained 3 weeks following the last chill revealed a normal liver.

Case 7. A 22-year-old man gave a history of shaking chills and fever, occurring every other day, while on board ship returning from Korea. One week later he noted anorexia, nausea, vomiting, and dark urine. A blood smear on board ship was reported as showing malaria, type not stated, and he was treated with chloroquine. He had a past history of chills and fever a year previously, successfully treated with chloroquine, although the diagnosis of malaria was not established at that time. On arrival at this hospital, 11 days after the onset, his temperature was 99.4° F. Repeated blood smears for malaria were negative. His hemoglobin was 11.8; serum bilirubin, 0.5 mg. per 100 cc.; thymol turbidity, 18; cephalin-cholesterol flocculation, 3 plus; prothrombin activity, 65 percent; serum cholesterol, 103 mg. per 100 cc.; cholesterol esters, 52 mg. per 100 cc.; serum albumin, 3.3 grams per 100 cc.; and serum globulin, 4.7 grams per 100 cc. His temperature dropped to normal immediately after admission and he remained asymptomatic without further treatment for the malaria. His liver profile returned to normal about 2 weeks after admission. A liver biopsy specimen taken on the twelfth hospital day revealed a normal liver.

Case 8. A 30-year-old man spent 11 months in Leyte in 1945, where he had an episode of fever, anorexia, dark urine, and jaundice which was treated with rest for 10 days. In January

1951, while on maneuvers in Louisiana, he noted the sudden onset of fever, with a temperature of 104° F., and generalized aching pain. He was hospitalized. One week later he became deeply jaundiced and a diagnosis of infectious hepatitis was made. He improved slowly and was not returned to duty until 28 July. On 24 August he was again hospitalized because of persistent pain in the right upper abdominal quadrant, appearing particularly with physical activity. Examination revealed a palpable and tender liver. Liver function tests were normal, but cirrhosis of the liver was considered and he was transferred to this hospital for further study. Examination here also revealed a slightly tender liver palpable 3 cm. below the right costal margin, a mild cervical and inguinal lymphadenopathy, and a temperature of 98° F. Blood smears disclosed *P. vivax*. His hemoglobin was 15.1; serum bilirubin, 0.5 mg. per 100 cc.; thymol turbidity, 6; cephalin-cholesterol flocculation, negative; serum cholesterol, 294 mg. per 100 cc.; serum albumin, 6.3 grams per 100 cc.; serum globulin, 3.4 grams per 100 cc.; and bromsulphalein retention, 1 percent in 45 minutes. A cholecystogram was normal. Repeated stool examinations failed to reveal any parasites or ova. Rectal biopsy showed no evidence of schistosomiasis. The patient remained afebrile. He was treated with chloroquine, following which his liver was no longer palpable and the malarial parasites disappeared from his blood. On discharge from the hospital he still complained of vague discomfort in the right upper abdominal quadrant, but this was much less marked than on admission.

A liver biopsy specimen obtained prior to the chloroquine therapy revealed small amounts of brown pigment in the cytoplasm of a few of the parenchymal cells and small foci of mononuclear cells scattered throughout the liver lobules (fig. 4). The Armed Forces Institute of Pathology reported minimal histologic changes of undetermined cause.

DISCUSSION

Although this small series of patients with malaria is not statistically significant, it was hoped that comparing them with a group of patients with hepatitis would indicate differences suggesting lines for future profitable study. The zinc sulfate turbidity, thymol turbidity, cephalin-cholesterol flocculation, urine urobilinogen, and serum proteins were not significantly different in the 2 groups. The serum cholesterol averaged somewhat lower in the patients with malaria, but there was an overlap in the individual values. The initial serum bilirubin also tended to be lower in the patients with malaria, although low or even normal levels may occur in hepatitis.

The hemoglobin in the malarial patients 1 and 2 was normal, but the serum bilirubin level was moderately elevated. We believe that both of these patients had concomitant malaria and viral hepatitis. In malarial patients 3 and 4, the hemoglobin was markedly lowered and the serum bilirubin level was slightly elevated. These probably represent the effect of extensive

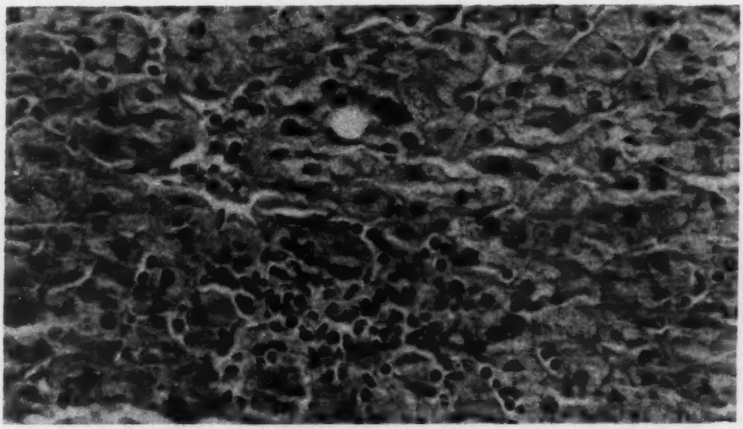

Figure 4. Section of liver. Note the minute collection of mononuclear cells.

hemolysis with the production of bilirubin exceeding the capabilities for excretion. In malarial patients 5 and 6 the hemoglobin was slightly on the low side of normal and the serum bilirubin level was slightly elevated. The bilirubinemia in these patients may have been secondary to hepatocellular damage caused by the malaria, but slight hemolysis or other factors cannot be excluded. In malarial patients 7 and 8, the serum bilirubin was normal. The cases presented do not particularly show that jaundice occurs in patients with malaria in the absence of significant hemolysis.

The liver biopsy specimens were obtained rather late in some of these patients, reducing to some extent the significance of the results (table 4). The only specimens revealing the histologic picture of hepatitis were those obtained from patients 1 and 2. Clinically, both of these were thought to have hepatitis with superimposed malaria. Patient 4 had clinical evidence of severe hemolysis which was further substantiated by the histologic findings in the liver. Patient 3 had severe hemolysis similar to patient 4, yet the liver specimen appeared normal. This is probably accounted for by the fact that the specimen was taken following a recurrence of malaria many weeks after recovery from the anemia. The liver specimen in patient 8 disclosed the un-

usual findings of a small amount of brown, granular pigment in some of the parenchymal cells and small foci of round cells scattered through the liver lobules. These changes were not those usually associated with hepatitis and presumably were caused by the malaria. The pigment may have remained from the hemolysis occurring earlier during the acute phase of the disease. In general, there appeared to be fewer morphologic changes in the liver of patients with malaria than in those with hepatitis.

TABLE 4. *Results of liver biopsy in 8 patients with malaria*

Patient	Number of days after last chill	Clinical diagnosis	Pathologic diagnosis
1	2	Malaria and hepatitis	Hepatitis
2	7	Malaria and hepatitis	Hepatitis
3	2	Malaria	Normal liver
4	13	Malaria	Consistant with hemolysis
5	6	Malaria	Normal liver
6	21	Malaria	Normal liver
7	16	Malaria	Normal liver
8	Prior to treatment	Malaria	Minimal changes

We were unable to rule out concomitant malaria and viral hepatitis in this series. In patients 1 and 2, both diseases were almost certainly present. Although the symptoms in the remaining 6 patients simulated those of hepatitis in many ways, the lower serum bilirubin level and the absence of histologic findings of hepatitis in the liver specimens suggested that malaria was the only etiologic factor. The importance of making the correct diagnosis was more than academic because the treatment of the two conditions is different. Patient 8, for example, was treated for hepatitis for 8 months. Chronic malaria may have been the only disease, in which event earlier treatment of this condition would have saved months of hospitalization and disability.

SUMMARY

A study of 8 selected patients with vivax malaria and 20 unselected patients with viral hepatitis suggests that in some cases malaria may closely simulate viral hepatitis. The most consistent distinguishing features of malaria were: the demon-

stration of the malarial parasite; the less marked elevation of the serum bilirubin level; and the absence of the characteristic histologic findings of hepatitis, as shown in needle biopsy specimens of the liver.

BOOKS RECEIVED

Cardiac Therapy, by *Harold J. Stewart,* M. D., Associate Professor of Medicine, Cornell University Medical College, New York; Attending Physician, New York Hospital; Head of Division of Cardiology, Department of Medicine, New York Hospital-Cornell Medical Center. 622 pages; illustrated. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1952. Price $10.

The Old Egyptian Medical Papyri, by *Chauncey D. Leake,* Vice-President, University of Texas—Medical Branch, Galveston. Logan Clendening Lectures on the History and Philosophy of Medicine, Second Series. 108 pages. University of Kansas Press, Lawrence, Kans., publishers, 1952. Price $2.

Sterility, Its Cause and Its Treatment, by *J. Jay Rommer,* A. B., Ph. G., M. D., A. I. C. S., Gynecological Staff, Beth Israel Hospital, Newark, N. J.; Member; American Genetics Association, American Society for the Study of Sterility, New Jersey Neuropsychiatric Association, Fellow, New Jersey Obstetric and Gynecological Society. Part I-The Infertile Female, Part II-The Infertile Male. 424 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $12.50.

Zinsser's Textbook of Bacteriology, by *David T. Smith,* M. D., Professor of Bacteriology and Associate Professor of Medicine, Duke University School of Medicine; *Norman F. Conant,* Ph. D., Professor of Mycology and Associate Professor of Bacteriology, Duke University School of Medicine; *Joseph W. Beard,* M. D., Professor of Surgery in charge of Experimental Surgery, Duke University School of Medicine; *Hilda Pope,* Ph. D., Assistant Professor of Bacteriology, Duke University School of Medicine; *D. Gordon Sharp,* Ph. D., Assistant Professor of Biophysics in Experimental Surgery, Duke University School of Medicine; and *Mary A. Poston,* M. A., Instructor in Bacteriology, Duke University School of Medicine. 10th edition. 1,012 pages; illustrated. Appleton-Century-Crofts, Inc., New York, N. Y., publishers, 1952.

Diabetic Glomerulosclerosis, The Specific Renal Disease of Diabetes Mellitus, by *Harold Rifkin,* M. D., F. A. C. P., Lecturer in Medicine, College of Physicians and Surgeons, Columbia University; Adjunct Attending Physician, Medical Division, Montefiore Hospital; Associate in Medicine and Assistant Professor, Department of Bacteriology, Flower-Fifth Avenue Hospitals, New York Medical College, New York, N. Y., *Louis Leiter,* M. D., Ph. D., Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University; Chief, Medical Division, Montefiore Hospital, New York, N. Y., and *James Berkman,* M. D., Instructor in Pathology, College of Physicians and Surgeons, Columbia University; Associate Pathologist, Montefiore Hospital, New York, N. Y. 102 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1952.

EPIDEMIC HEMORRHAGIC FEVER[1]

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EPIDEMIC hemorrhagic fever is unfamiliar to most clinicians in the United States. It was first described in 1939 by Japanese military physicians stationed in the Songo district of Manchuria (2, 3). The disease also occurred in members of the Russian Army units operating along the Manchurian border (4). In 1943 the Japanese Army Medical Corps recognized the disease as an entity and officially named it epidemic hemorrhagic fever. The Japanese believed that it was caused by a virus; that the reservoir was the field mouse *Apodemus agrarius;* and that the vector was the mite, *Laelaps jettmari vitzthum.* Their data on the cause and transmission of the disease have as yet neither been confirmed nor disproved.

In June 1951 we began to observe patients in whom the clinical manifestations and the gross pathologic findings were consistent enough, from case to case, to indicate that we were dealing with a disease entity (5, 6). The consensus at that time was that we were dealing with an atypical form of leptospirosis and we were further misled by the erroneous identification of artefacts as leptospira in dark-field preparations of the serum of acutely ill and recently deceased patients. We were shortly disillusioned.

The microscopic studies on the tissues of animals injected with blood and urine of acutely ill patients and the postmortem tissues of human cases revealed no leptospira. Serial agglutin-

(1) From the Medical Service, 121st Evacuation Hospital, Korea.

(2) Takami, R. M.: Epidemic hemorrhagic fever. Mimeographed report of consolidated translations. Medical Section, GHQ, FEC, 13 Aug. 1951.

(3) Craig, J. P.: Epidemic hemorrhagic fever. Mimeographed report. 406th Medical Laboratory, Feb. 1951.

(4) Diathesis hemorrhagic and icterohemorrhagic leptospirosis. In Experience of Soviet Medicine in the Great War for the Fatherland. State Publishing House for Medical Literature. Vol.24, chap. 3.

(5) Hornisher, C. J.: Epidemic hemorrhagic fever. Surgeon's Circular Letter, GHQ, FEC, VI, 10 Nov. 1951.

(6) Inmon, T. W.: Epidemic hemorrhagic fever. Information Bulletin, Office of the Surgeon, Hq EUSAK. 29: 1, 1 Sept. 1951.

ations were not diagnostic for leptospirosis. The final blow to a diagnosis of leptospirosis was the demonstration of spiral forms in the dark-field studies performed on serums from normal persons who had had no possible exposure to the disease in the area from which we were receiving patients. All of the possibilities mentioned in the differential diagnosis were explored and discarded for want of objective confirmation. Having thus explored the familiar we were then prepared to explore the unfamiliar.

In February 1951 we had received a brief translation of Japanese descriptions of epidemic hemorrhagic fever from the 406th Medical General Laboratory in Japan. The manifestations of the disease in our patients were essentially the same as those described by the Japanese workers. From late June through early October we observed over 180 patients whose illnesses were sufficiently typical to permit a diagnosis of epidemic hemorrhagic fever. Our observations on these patients form the basis for this article.

SYMPTOMS

Epidemic hemorrhagic fever is usually abrupt, but may be insidious in its onset. A prodromal stage lasting 1 or 2 days may occur with grippal symptoms, mild diarrhea, and general malaise. This is followed in rapid sequence by chills, fever, retrobulbar headaches, myalgia, and joint pains. Anorexia is present from the onset. Nausea and vomiting begin about the second day and persist for about a week. As the hemorrhagic tendency becomes more pronounced, hematemesis, hemoptysis, hematuria, and bloody diarrhea may appear. Abdominal pain is a constant complaint; it may be periumbilical or lower, but is most common in the upper abdominal quadrants. Sedation may be necessary for its relief. Low back pains and testicular pain may be present. Hiccuping is an exhausting and annoying symptom. Most patients are restless, tense, and complain of insomnia and nightmares. Headache in the first 3 days is associated with transient periods of photophobia, blurring of vision, and myopia. Oliguria persists throughout the acute stage.

With convalescence a sudden diuresis may occur followed by urinary urgency and frequency, nocturia, and polydipsia of about 1 week's duration. Concurrently the appetite is ravenous. The duration of the disease is 1 or 2 weeks and in most patients recovery is complete in 3 weeks. Prolonged renal insufficiency has been noted in patients with a past history of nephritis. Occasionally stuttering is a sequela. Hemorrhages and ecchymosis disappear in 3 or 4 weeks. One of the outstanding features of the disease is the increase in severity of clinical signs and symptoms coincident with the disappearance of fever.

PHYSICAL FINDINGS

The patient appears acutely ill from the onset of the disease until convalescence begins. The temperature rises abruptly to about 104° F., remains high for 3 or 4 days, then usually returns to normal by the seventh day. The skin of the face, neck, and chest is deeply flushed. The face and periorbital tissues are swollen and edematous. The skin is dry, perspiration appearing only with the onset of shock. A fine petechial rash may be seen on the chest, axilla, and wherever the clothing is tight. The pharynx is injected. The Rumpel-Leede sign is positive in 3 or 4 minutes.

The bulbar and palpebral conjunctivas are suffused at the onset, later become injected, and small petechias occur which may coalesce forming ecchymosis. Subconjunctival hemorrhage is one of the most frequent objective findings in our patients, but we have not observed the hemorrhagic involvement of the uvea and retina described by the Japanese workers. Epistaxis and bleeding from the gums are difficult to control. Ecchymosis appears at all sites of trauma to the skin. A single injection of medication, a tourniquet, or a sphygmomanometer cuff may cause ecchymosis of an entire extremity.

The physical findings of pneumonitis and pulmonary edema may be evident. Dyspnea and cyanosis due to pulmonary hemorrhage and consolidation pose a therapeutic problem. A fulminating pneumonia may result in death within 2 or 3 hours. A tachycardia accompanies the fever but cardiac arrhythmias are rare. Despite the abdominal pain, there is no localized tenderness. The liver and spleen are usually not palpable. The abdomen may become distended due to ileus. Deep palpation should be avoided because of the danger of increasing internal hemorrhage. At autopsy, rupture of the spleen and ecchymotic areas of the diaphragm, liver, stomach, bowel, and mesentery have been noted. In some fatal cases a sudden shocklike state may make its appearance, with marked peripheral vascular collapse. The pulse is rapid, the blood pressure is imperceptible; and the patient becomes cyanotic and restless. Such a patient may die within 2 or 3 hours. At autopsy gross pituitary hemorrhages are present.

LABORATORY FINDINGS

Urine. Albuminuria of from 1 to 4 plus appears within from 28 to 72 hours, persists for 1 week, and subsides during the ensuing 2 weeks of convalescence. The specific gravity falls to from 1.002 to 1.005 in the first week of illness and the patient regains his ability to concentrate during the 2 weeks of convalescence. Microscopic to gross hematuria is present early

but usually clears within 2 weeks. Granular, waxy, and erythrocytic casts accompany clinical improvement.

Blood. The leukocyte count is normal or a leukopenia may be present early to be followed by a rapidly rising count within the following 2 or 3 days. In most patients the count reaches about 30,000 but occasional counts of 100,000 are seen. In some patients the leukocytosis may last only 48 hours. The

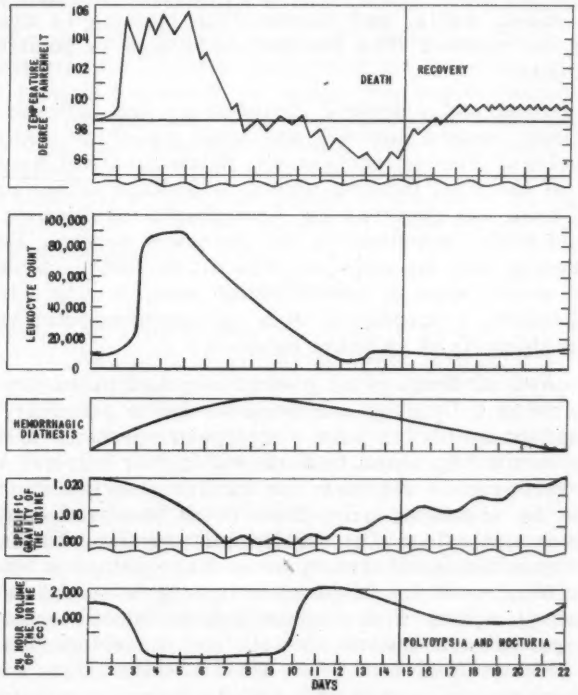

Figure 1. Graphic representation of time relationships of various manifestations.

differential count is 70 to 80 percent neutrophils; 15 to 20 percent lymphocytes; and 5 to 10 percent monocytes. About 25 percent of the lymphocytes are atypical. There is a relative absence of eosinophils during the acute phase of the disease, but they appear again on convalescence. We have not observed the eosinophilia described by the Japanese workers.

There is a decrease in platelets to about 100,000 per cu. mm. in the first week, then a return to normal. The erythrocyte count, hemoglobin, and hematocrit are above normal levels in the same period. Bleeding, coagulation, and clot retraction times are

normal. The patients' prothrombin time is from 20 to 40 seconds (control 14), returning to normal in 2 weeks.

Blood chemistry. The nonprotein nitrogen is elevated by about the sixth day to from 60 to 80. It returns to normal as the kidneys regain their ability to concentrate urine.

Serology. The serologic test for syphilis, Weil-Felix and Widal agglutinations, and heterophile antibody reaction are negative. Agglutination against 12 strains of leptospira has also been repeatedly negative. Dark-field examination of the blood and urine is negative for leptospira and borrelia. Malarial smears are occasionally positive, but treatment of the malaria does not alter the course of the disease. The sedimentation rate is not increased at the onset but may show a slight rise later.

Spinal puncture may reveal normal or bloody fluid. The pressure is normal.

Figure 1 shows the time relations of various manifestations.

DIAGNOSIS

As in most infectious diseases, the severity and duration of the symptoms and signs are variable from patient to patient. On the other hand, some objective findings are observed consistently enough to form a reasonable basis for diagnosis. The most consistent objective findings are subconjunctival hemorrhage, leukemoid leukocytosis, oliguria, and albuminuria. An increase in the severity of these and other signs coincident with defervescence is also diagnostic.

In the differential diagnosis the following diseases should be ruled out: (1) leptospirosis, (2) purpura, (3) acute meningococcemia, (4) hemorrhagic smallpox, (5) sand fly fever, (6) subacute bacterial endocarditis, (7) relapsing fever, (8) epidemic typhus, (9) acute myelogenous leukemia, and (10) drug and chemical poisoning.

COMPLICATIONS

Complications include parotitis, orchitis, pancreatitis, hepatitis, encephalitis, and bladder paralysis. Recovery of the ability to concentrate urine is delayed in some patients.

PROGNOSIS

In patients with a past history of renal disease, convalescence may be prolonged. Obesity adversely affects the prognosis. The average patient can be returned to duty in about 3 weeks. The mortality is about 13 percent. The principal causes of death are hemorrhage into the pituitary, lungs, and kidneys; peripheral vascular collapse; and uremic coma. It is difficult to give a

prognosis because some patients who were very ill and seemed to be poor risks made a dramatic recovery within 24 hours and others who seemed only mildly ill died within 12 hours or less.

GROSS PATHOLOGY

The most frequent gross pathologic findings are hemorrhage and edema, which may involve any organ or system but are most commonly present in the kidney and surrounding retroperitoneal tissues, upper gastrointestinal tract, lungs, wall of the right atrium, and the pituitary and its stalk. The appearance of the kidney is striking. The medulla is dark red and hemorrhagic and the cortex is edematous and pale. This appearance was previously noted by Japanese workers as a consistent finding.

TREATMENT

The treatment, in general, is symptomatic and supportive. The clothing should be loose. Trauma accompanying injections, numerous laboratory procedures, and deep palpation should be avoided. A liquid diet is given. Cold liquids and carbonated beverages are fairly well tolerated in small quantities. Narcotics and sedatives are given as indicated. A maximum of 500 cc. of 10 percent dextrose in water containing 70 mg. of vitamin K and 200 mg. of vitamin C is administered intravenously. The tendency toward sudden edema renders fluid restriction mandatory during the first 7 to 10 days of the disease. ACTH and cortisone are given for shock as indicated, but the results have not been striking. Oxygen, blood, epinephrine, and other supportive measures are used as indicated. Transfusions of from 250 to 500 cc. of whole blood obtained from patients in their third week of illness were given to about 70 of our patients. It is our impression that this measure is helpful if administered during the first 5 days of the illness. It is emphasized that this is our impression and not a statistically supportable fact.

The following drugs and antibiotics have not proved beneficial: penicillin, streptomycin, aureomycin, terramycin, chloramphenicol, sulfadiazine, and 4-aminoquinoline compounds.

SUMMARY

Epidemic hemorrhagic fever is an acute infectious disease, possibly caused by a virus and characterized by an abrupt onset, chills, fever, retrobular headache, myalgia, vomiting, abdominal pain, hemorrhagic phenomena, leukocytosis, and albuminuria, and increase in symptoms and signs with defervescence. The lesions consist predominately of hemorrhages involving any system or combination of systems but most frequently the kidney, pituitary, muscles, and gastrointestinal tract. No distinctive microscopic lesions have been recognized.

CLINICAL SIGNIFICANCE OF ANTI-RH ANTIBODY DETERMINATIONS (1)

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ALTHOUGH the recent literature contains innumerable reports concerning the various Rh and Hr agglutinogens, there still remains much confusion as to the clinical significance and application of anti-Rh antibody determinations. Anti-Rh antibodies are not normally present in the blood. They occur only as a result of immunization. Immunization is produced by the introduction of Rh agglutinogens into susceptible persons, usually as a result of pregnancies or transfusions. The intramuscular injection of blood as previously practiced for therapeutic purposes may also produce immunization. One instance of sensitization due to the intramuscular injection of human serum has been reported by Wallace et al. (2).

Wiener and Sonn-Gordon (3) have immunized male volunteers by only 2 successive parenteral injections of Rh agglutinogens. Although the interval of rest between these injections was 4 months, they found this would produce immunization in only 40 percent of the persons tested. These workers postulated that 1 injection was necessary to prime the reticuloendothelial system, then after 3 or 4 months of rest the second injection would result in antibody formation if the person were susceptible. It is estimated that there is a 1:3 chance of fetal blood passing into the maternal circulation during pregnancy and a 1:3 chance during parturition (4). As would be expected, primigravidas without previous injections of Rh agglutinogens rarely deliver erythroblastotic infants.

Three varieties of anti-Rh antibodies are generally recognized: saline-active agglutinins, serum-albumin agglutinins, and block-

(1) U. S. Naval Hospital, Oakland, Calif.

(2) Wallace, J. T.; Wiener, A. S.; and Doyle, M. H.: Rh sensitization in primipara caused by intramuscular injection of human serum resulting in fatal erythroblastosis. Am. J. Obst. & Gynec. 56: 1163-1167, Dec. 1948.

(3) Wiener, A. S., and Sonn-Gordon, E. B.: Simple method of preparing anti-Rh serum in normal male donors. Am. J. Clin. Path. 17: 67-70, Jan. 1947.

(4) Wiener, A. S.; Nappi, R.; and Gordon, E. B.: Studies in Rh sensitization; effect of Rh-positive pregnancies on Rh antibody titer. Blood 6: 789-798, Sept. 1951.

ing antibodies. The saline-active agglutinins will agglutinate Rh-positive cells suspended in saline solution. The serum-albumin agglutinins agglutinate Rh-positive cells suspended in serum albumin. Blocking antibodies are attached to the erythrocytes but do not produce clumping and are detected by means of an indicator. A possible fourth variety, the cryptagglutinoids, as described by Hill et al. *(5)*, are globulin antibodies which coat the erythrocytes and react with rabbit antihuman globulin serum. This is the antibody demonstrable by the Coombs test. All types act in vitro to produce agglutination whereas in vivo they result in hemolysis.

Diamond and Denton *(6)* stated that saline agglutinins are the first to appear as a result of sensitization whereas serum-albumin agglutinins and blocking antibodies are evident only after prolonged immunization. The more severe forms of hemolytic disease are usually found in the offspring of women whose blood contains serum-albumin agglutinins and blocking antibodies. Wiener *(7)* postulated that the smaller blocking antibodies and serum-albumin agglutinins traverse the placenta more readily than the larger saline-active agglutinins. He found an 8 percent incidence of stillbirths associated with maternal serums containing high titers of only saline-active agglutinins. Maternal serums having high titers of serum-albumin agglutinins and blocking antibodies were associated with a 43.9 percent incidence of stillbirths.

Davidsohn and Stern *(8)* found significant correlation between serum-albumin agglutinin titers, with or without blocking antibodies, and fetal death. They reported a 72 percent fetal salvage when the serum-albumin agglutinin titers were less than 1:10 and blocking antibodies were not present. If blocking antibodies were present the salvage was reduced to 57 percent. When the maternal serums contained titers of serum-albumin agglutinins in excess of 1:10 without blocking antibodies, only 39 percent of the infants survived. If, however, blocking antibodies were present, this salvage was reduced to 28 percent.

Page et al. *(9)* found that the duration of exposure of the fetus to maternal antibodies was of possible prognostic value. All stillbirths in the patients they investigated were associated with

(5) Hill, J. M.; Haberman, S.; and Jones, F.: Hemolytic Rh immune globulins; evidence for possible third order of antibodies incapable of agglutination of blocking. Blood, Spec. Issue No. 2, pp. 80-100, Jan. 1948.

(6) Diamond, L. K., and Denton, R. L.: Rh agglutination in various media with particular reference to value of albumin. J. Lab. & Clin. Med. 30: 821-830, Oct. 1945.

(7) Wiener, A. S.: Pathogenesis of erythroblastosis fetalis; statistical evidence. Am. J. Clin Path. 16: 761-767, Dec. 1946.

(8) Davidsohn, I., and Stern, K.: Interpretation of Rh antibodies. Am. J. Clin. Path. 18: 690-699, Sept. 1948.

(9) Page, E. W.; Hunt, M. L.; and Lucia, S. P.: Antepartum prediction of hemolytic disease of newborn. Am. J. Obst. & Gynec. 52: 794-796, Nov. 1946.

demonstrable antibodies in the maternal serum for a period of 15 weeks or more prior to delivery.

Once established, maternal immunization is permanent and all Rh-positive children born after the delivery of 1 erythroblastotic infant will usually manifest hemolytic disease *(10)*. Davidsohn *(11)* found the titer of anti-Rh agglutinins in the blood of mothers with erythroblastotic children to be highest from 8 to 20 days following delivery. Wiener et al. *(12)* found that all sensitized persons presented antibodies for at least 4 years following delivery when enzyme-treated cells were used in the determinations. Halac *(13)* was able to demonstrate antibodies in 1 patient 33 years following her last pregnancy.

At this hospital, 2,678 patients were delivered in 1951. Three hundred and thirty-one (12.4 percent) of these were Rh_0 negative. There were 39 Rh_0-negative patients married to Rh_0-negative husbands, which approximates the expected ratio of 1:7. There were 190 multigravidas and 141 primigravidas. Anti-Rh antibody determinations were performed on all Rh-negative patients married to Rh-positive husbands at every prenatal visit regardless of previous pregnancies or transfusions. Many of these patients were followed elsewhere and seen at this hospital only during the last 4 weeks of pregnancy.

PROCEDURE FOR ANTI-RH ANTIBODY DETECTION

An approximate 1 percent cell suspension was prepared from 5 or more group "O" Rh_0-positive specimens of fresh clotted blood. These cells were suspended in pooled fresh plasma which was fortified with 25 percent concentrated albumin. Aliquots of each cell suspension were incubated for 2 hours at 37° C. and shaken intermittently. After incubation, a large drop of the contents of each tube was transferred to a Boerner slide. This was rotated for 10 minutes, then read microscopically. Both a positive and a negative serum control were included. If this presumptive test was positive, the serum was titrated by making serial dilutions with the fortified plasma diluent. The pooled type "O" Rh_0-positive cells were added to the serum dilutions and incubated for 2 hours.

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(10) Potter, E. L.: Rh: Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions. Year Book Publishers, Inc., Chicago, Ill., 1947.

(11) Davidsohn, I.: Rh antibodies. Am. J. Clin. Path. 15: 95-105, Mar. 1945.

(12) Wiener, A. S.; Nappi, R.; and Gordon, E. B.: Studies in Rh sensitization; persistence of Rh antibodies in serum of sensitized individuals. Blood 6: 799-803, Sept. 1951.

(13) Halac, E.; Linares Garzón, H.; and Ottero de Sacchetti, M. O.: Isoimmunización por el factor Rh; estudio sobre su duracion en estado activo. Arch. argent. de. pediat. 30: 1-9, 1948. Cited in footnote reference *(12)*.

RESULTS

Of the 331 Rh-negative patients, only 11 were found to be sensitized. The case histories of these are briefly summarized.

Case 1. The estimated date of confinement of a 31-year-old white para 3 gravida 5 abortus 1 was 10 September 1951. The last child had icterus at birth but required no treatment. The husband and the 3 children were Rh_o positive. There was no history of previous transfusions. The patient was first seen at this hospital in labor on 6 July. An anti-Rh antibody determination on admission was reported as 1:2,008. She delivered a hydropic stillborn infant. Autopsy confirmed the diagnosis of erythroblastosis.

Case 2. The estimated date of confinement of a 29-year-old white para 2 gravida 3 was 14 February 1951. The second child required 2 transfusions for anemia following delivery. The husband and the 2 children were Rh_o positive. The patient was reported to be Rh_o positive on 2 occasions at other clinics. On 21 February the fetus died in utero and on 22 February she delivered a hydropic stillborn infant which at autopsy was found to be erythroblastotic. Re-examination revealed the patient to be Rh_o negative with a titer of 1:512. An anti-Rh antibody titration performed on 13 March 1952 was also reported as 1:512.

Case 3. The estimated date of confinement of a 30-year-old white para 2 gravida 3 was 13 November 1951. The second child had presented icterus at birth but required no therapy. The husband and the 2 children were Rh_o positive. Anti-Rh antibody titers were as follows: 18 July, negative; 15 August, 7 and 21 September, 1:16; and 5, 12, 19, and 26 October, 1:256. On 2 November she entered the hospital in labor. The fetal heart tones were absent. A stillborn hydropic infant was delivered which at autopsy presented the findings of erythroblastosis.

Case 4. The estimated date of confinement of a 24-year-old white para 3 gravida 4 was 19 February 1951. Her husband and 2 children were Rh_o positive. One child was Rh_o negative. The patient had received no transfusions and all 3 children had presented no evidence of hemolytic disease. On 14 February an antibody titer was reported as 1:64 and 6 days later the titer was 1:8. On 21 February she delivered a normal Rh_o-negative infant.

Case 5. The estimated date of confinement of a 30-year-old white para 2 gravida 3 was 17 May 1951. This patient had received a transfusion of type "O" Rh-negative blood following the

delivery of her first child in 1947. Her husband and 2 children were Rh_o positive. Antibody titers were as follows: 4, 10, and 18 April, 1:64; 26 April and 3 May, 1:256; and 4 and 6 May, 1:128. Beginning on 10 April, treatment with 25 mg. of cortisone every 6 hours was started. The patient received a total of 2,500 mg. On 7 May labor was induced by amniotomy. An icteric boy who had a hemoglobin of 12.5 grams with 3.5 million erythrocytes was delivered. There were 191 nucleated erythrocytes per 100 leukocytes. An exchange transfusion of 500 cc. of type "O" Rh_o-negative blood was given 2 hours following delivery through the umbilical vessels. The baby was also given cortisone as follows: 8 mg. every 6 hours for 8 doses; 6 mg. every 4 hours for 2 doses; 4 mg. every 6 hours for 3 doses; and 2 mg. every 6 hours for 2 doses. He was discharged in good condition on 24 May, which was the seventeenth day of life. On 16 June his hemoglobin was found to be 6.5 grams with 3.3 million erythrocytes. He was given 75 cc. of blood on 2 successive days. He was discharged with a hemoglobin of 12 grams and 4.3 million erythrocytes. The anemia has not recurred. The mother's antibody titer 6 weeks postpartum was 1:8,192.

Case 6. The estimated date of confinement of a 23-year-old white para 1 gravida 4 abortus 2 was 29 July 1951. She had received no transfusions and her living child apparently had been normal. Antibody titers were as follows: 13 and 20 July, negative; and 27 July, 1:4. On 27 July she delivered an icteric infant who had a hemoglobin of 13 grams and 4.3 million erythrocytes. There were 7 nucleated erythrocytes per 100 leukocytes. No treatment was given and the infant recovered uneventfully.

Case 7. The estimated date of confinement of a 24-year-old white para 2 gravida 3 was 7 September 1951. Her husband and 2 children were Rh_o positive. The children had had no evidence of erythroblastosis. Antibody titers were as follows: 2 and 7 August, negative; 21 August, doubtful; and 19 September, 1:64. On 19 September the patient delivered an icteric infant who had a hemoglobin of 15 grams and 5.8 million erythrocytes. No nucleated cells were present. On 22 September the hemoglobin was 14 grams with 4.8 million erythrocytes. Icterus was increasing and 80 cc. of blood were given. The child was discharged on 27 September in good condition.

Case 8. The estimated date of confinement of a 39-year-old white para 4 gravida 5 was 30 January 1951. Her husband was Rh_o positive and the other children had had no evidence of hemolytic disease. Antibody titers were as follows: 13 December 1950, questionable; 8 January 1951, 1:16; 10 January, 1:8; 17 January, 1:16; and 24 January, 1:64. On 30 January the patient

delivered an icteric infant who had 13 grams of hemoglobin and 4.1 million erythrocytes. There were 5 nucleated erythrocytes per 100 leukocytes. Two hours after birth an exchange transfusion of 425 cc. of type "A" Rh_0-negative blood was given. On 31 January an additional 90 cc. of blood were given. The child made an uneventful recovery and was discharged on 14 February.

Case 9. The estimated date of confinement of a 19-year-old white para 0 gravida 1 was 21 October 1951. A left nephrectomy had been performed elsewhere after 3 months' gestation and a transfusion had been given. This patient was transfused with "O" Rh_0-positive blood. Her husband was Rh_0 positive. Antibody titers were as follows: 22 June, negative; 27 July, questionable; 17 August, 1:64; 31 August, and 7 and 14 September, 1:128; 21 and 28 September, and 5, 12, and 19 October, 1:256; and 24 October, 1:64. The patient delivered an apparently normal infant on 24 October, but the infant's serum contained anti-Rh antibodies. Icterus developed on the first day of life and the hemoglobin was found to be 14.5 grams with 5.1 million erythrocytes. No nucleated erythrocytes were present. The icterus did not increase and on 27 October the hemoglobin was 16 grams and there were 5.6 million erythrocytes. The infant was discharged in good condition. On 13 March 1952 examination of the maternal serum revealed an antibody titer of 1:64.

Case 10. The estimated date of confinement of a 26-year-old white para 2 gravida 3 was 30 December 1951. Her husband was Rh_0 positive and her 2 children had been apparently normal. Antibody titers were as follows: 30 November and 7 December, negative; and 14 December, 1:128. Labor was induced by amniotomy on 20 December. She delivered on the same day and an antibody titer following delivery was reported as 1:1,024. This infant had a mild icterus. The hemoglobin was 9.5 grams with 3.2 million erythrocytes. There were 52 nucleated erythrocytes per 100 leukocytes and the infant's serum had an anti-Rh antibody titer of 1:16. A transfusion of 75 cc. of type "A" Rh-negative blood was given and the hemoglobin increased to 14 grams with 4.7 million erythrocytes. There were, however, 180 nucleated erythrocytes per 100 leukocytes. On 22 December the icterus had increased and edema developed. An exchange transfusion was started but the infant died during the procedure. Autopsy confirmed the diagnosis of erythroblastosis and, in addition, atelectasis was present.

Case 11. The estimated date of confinement of a 21-year-old white para 0 gravida 1 was 10 July 1951. Her husband was Rh_0 positive. She had received no transfusions. Antibody titers were

as follows: 9 May, negative; 13 June, 1:32; 20 June, 1:2; and 27 June and 6 July, 1:4. She delivered a normal infant on 16 July who showed no evidence of hemolytic disease. The Rh factor was not determined for the infant.

DISCUSSION

Of the 2 primigravidas in this series, 1 had received blood. The other gave no history of previous blood transfusion, but the intramuscular injection of blood during infancy could not be excluded. Only 2 of the sensitized patients in this series delivered normal infants. Case 4 delivered an Rh-negative infant and the demonstrable antibodies probably were a carry-over from a previous pregnancy, or this could be an instance of an anamnestic reaction. The Rh_0 factor was not determined in the other infant whose mother's antibody titrations never exceeded 1:32. No infants were delivered in this 1-year period with hemolytic disease due to Rh incompatibility in which anti-Rh antibodies were not demonstrable in the maternal serum.

Of the 9 infants exhibiting hemolytic disease, 3 were hydropic stillbirths. The mothers of these 3 had serum-albumin agglutinins and blocking antibody titers of 1:256 or higher. The remaining 8 patients had titers of 1:256 or less. Four of these infants required multiple or exchange transfusions. Only one infant expired and it might have survived had exchange transfusions been performed immediately after birth.

One patient (case 5) received cortisone therapy during the last 4 weeks of her pregnancy. Her infant was treated with cortisone as well as with an exchange transfusion.

The significance of a single antibody determination is difficult to interpret. Repeated examinations are necessary in order to predict the possible presence of hemolytic disease in the infant and, in some cases, the severity of the disease. Even with repeated examinations, an accurate prognosis may be difficult. An increasing antibody titer may not signify that the pregnancy will terminate in the delivery of an infant with hemolytic disease. An Rh-negative infant in utero can result in a rising maternal titer by producing an anamnestic reaction *(14)*. On the other hand, a persistently low titer may not indicate the delivery of an infant free of erythroblastosis, but, in general, constant and marked titer increases are associated with erythroblastotic infants. A titer that suddenly drops may be of great significance. This may indicate fetal death or increased absorption of antibodies by the fetus or placenta, but in anamnestic reactions and with carry-

(14) Schneider, C. L.: Frequency of Rh anamnestic reaction during pregnancy. Am. J. Obst. & Gynec. 59: 371-377, Feb. 1950.

over antibodies from previous immunizations, titer decreases may be of no prognostic significance.

An absolute prediction of the survival of a fetus in utero cannot be made on the basis of antibody determinations. Antibody titrations will, however, suggest the possibility of hemolytic disease being present in the newborn so that adequate preparation can be made for the care of these infants following delivery. In selected cases, labor can be induced near term. The elective termination of pregnancy prior to the thirty-sixth week of gestation on the basis of antibody determinations is unwarranted.

Antibody determinations are indicated in all Rh-negative maternity patients who are married to Rh-positive husbands. Primigravidas without previous blood transfusions may have had intramuscular injections of blood and it may be difficult to elicit a history of self- or criminally-induced abortion. For correct interpretation, an antibody determination should be made early in pregnancy. Antibodies which are found during the first trimester are as a rule the result of previous immunization. Another determination should be made during the thirty-third or thirty-fourth week and another during the thirty-eighth week of pregnancy. If a patient presents evidence or a history of immunization, anti-Rh antibody titrations are indicated every 2 weeks until the last month of pregnancy, then twice weekly. Davidsohn *(15)* recommends determinations at 1- or 2-month intervals until the seventh month, then at biweekly intervals. Browne *(16)* makes antibody determinations only at monthly intervals during the last half of pregnancy in primigravidas and in multigravidas at monthly intervals after the fourth month of gestation.

SUMMARY

Three hundred and thirty-one (12.4 percent) of the obstetrical patients delivered at this hospital in 1951 were Rh_0 negative. Two hundred and twenty-nine of these Rh_0-negative patients were married to Rh_0-positive husbands. Eleven (4.8 percent) of these 229 patients were sensitized. Nine of these 11 patients delivered infants who had hemolytic disease. Three were hydropic stillbirths. Only 1 neonatal death occurred. The ultimate outcome of pregnancy could not be absolutely predicted on a basis of antibody determinations.

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(15) Davidsohn, I.: Rh antibodies; correlation with clinical findings. Blood, Spec. Issue No. 2, pp. 139-154, Jan. 1948.

(16) Browne, W. H.: Symposium on gynecology and obstetrics; present status of management of Rh-negative pregnant woman. S. Clin. North America 30: 169-174, Feb. 1950.

PSEUDOMONAS AERUGINOSA MENINGITIS

Report of Case Treated With Terramycin (1)

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WITH each new antibiotic the spectrum of unresponsive bacteria has been steadily narrowed. Among the bacteria still generally resistant to such treatment is *Pseudomonas aeruginosa*. Although not ordinarily a pathogen, it may cause infection if the resistance of the host is lowered. As Jawetz (2) pointed out, when the natural defenses of the body have not yet appeared, as in infants; have failed, as in debilitated persons; or when entrance is gained by the bacillus into areas lacking natural defenses, then infection, which is often chronic, disabling, and sometimes fatal, may result. *Ps. aeruginosa* has thus aptly been called an opportunist.

Invasion of the meninges by this organism results in a serious condition. The organism may be introduced by a lumbar puncture needle or less frequently by bacteremia from some focus of infection. The treatment of meningitis due to *Ps. aeruginosa* has been extremely difficult. The use of various antibiotics, including streptomycin and polymyxin, has met with varying success. The following case is reported because of the successful use of terramycin intravenously and because of various observations made during the treatment.

CASE REPORT

A 20-year-old man was admitted to this hospital on 29 November 1951. On 24 November, in North Korea, he was wounded in the left buttock by an enemy shell fragment. The wound was débrided under intravenous pentothal anesthesia and the patient was evacuated to Japan.

On admission physical examination revealed a wound of the lateral aspect of the left buttock, measuring 11 by 19 cm. and exuding purulent material. Wet dressings were applied to the wound and 300,000 units of procaine penicillin were given

(1) U. S. Army Hospital, 8163d Army Unit.

(2) Jawetz, E.: Infections with Pseudomonas aeruginosa treated with polymyxin. B. Arch. Int. Med. 89: 90-98, Jan. 1952.

intramuscularly every day. On 17 December the wound appeared to be ready for grafting and, under spinal anesthesia, a split-skin graft from the left thigh was placed on the wound. Postoperatively, the patient was given 500 mg. of terramycin by mouth, followed by 250 mg. every 6 hours for 3 days. Penicillin had been discontinued at the time of operation. Following operation, the patient developed mild headaches. He remained afebrile until the fourth postoperative day (1 day after the terramycin had been stopped) when his temperature rose to 99.8° F. It reached 100.4° F. on the fifth and 102.2° F. on the sixth postoperative day. At that time there was a minimal amount of purulent drainage at the margins of the grafted area. The leukocyte count was 12,400 with 51 percent polymorphonucleocytes, 31 percent lymphocytes, and 14 percent eosinophils, and 4 percent monocytes. Treatment with 500 mg. of aureomycin every 6 hours by mouth was started.

On the next day the patient was somewhat improved although he continued to run a low-grade fever. On the eighth postoperative day he began to complain of stiffness of the neck, pain over the lumbar puncture site, nausea, and vomiting. On the tenth postoperative day his rectal temperature was 103.6° F. and his headache, which had been present since the operation, became severe. He did not appear acutely ill, but there was stiffness of his neck and pain on flexion. There was no gross infection of the grafted wound, but a collection of serum was present under the graft. A lumbar puncture yielded cloudy fluid under a pressure of 250 mm. The spinal fluid cell count was 618, with 86 percent lymphocytes; the protein was 179 mg. per 100 cc.; the sugar was 22 mg. per 100 cc.; and no organisms were seen on smear. The patient was transferred to the medical service where it was decided to treat the patient for a bacterial meningitis, bearing in mind that the chemotherapy received postoperatively might have obscured the diagnosis. There was no evident source of infection. It was not thought that the wound had given rise to a septicemia. The possibility of infection having been introduced by the spinal anesthesia at the time of operation was considered.

A broad spectrum antibiotic, and preferably one which could be administered parenterally because of the nausea and vomiting, appeared to be indicated. Aureomycin was discontinued and 2 grams of terramycin in 2 liters of fluid was given intravenously in addition to 1 gram given orally in divided doses daily. On the next day (the eleventh postoperative day) the patient appeared slightly better. His rectal temperature was 101.6° F. Anorexia, nausea, and vomiting continued but his headache had ceased. The only positive physical findings were stiffness of the neck with pain on flexion and a questionable Kernig's sign. The remainder of the physical and neurologic examination was negative

except for complete loss of the skin graft. Lumbar puncture revealed a cloudy fluid with a cell count of 1,112 of which 96 percent were lymphocytes; the protein was 135 mg. per 100 cc.; the sugar was 20 mg. per 100 cc.; and no organisms were seen on smear. The intravenous and oral administration of terramycin was continued.

On the twelfth postoperative day the patient was still febrile and anoretic. He continued to have stiffness of the neck. A third lumbar puncture revealed a turbid fluid under increased pressure. The cell count was 1,200 with a predominance of lymphocytes. The spinal fluid sugar was 30 mg. per 100 cc.; the protein was 142 mg. per 100 cc.; and the smear revealed no organisms. During the next few days the patient improved. On the fourteenth postoperative day the second spinal fluid culture was reported as yielding *Ps. aeruginosa*. This organism was also cultured from the wound, but the sensitivities of the 2 cultures to antibiotics were different. The other spinal fluid cultures were negative. It seemed probable at the time that the spinal fluid growth might be a laboratory contaminant. The treatment with terramycin was continued.

The patient's fever steadily diminished and his symptoms disappeared except for nausea and vomiting. Because of the latter, the oral dose of terramycin was decreased on the seventeenth postoperative day. The stiffness of the neck slowly decreased. By the twenty-third postoperative day, the neck was supple and the temperature practically normal. Serial lumbar punctures on the fourteenth, sixteenth, eighteenth, and twenty-fourth days revealed a persistently turbid spinal fluid under a pressure of from 220 to 280 mm. The cell count fell to 612 with a preponderance of lymphocytes. The sugar rose slowly to 48 mg. per 100 cc. The Pandy reaction became 4 plus, and the protein rose to 474 mg. per 100 cc. Toward the end of the fourth postoperative week the patient looked very well. There was some drainage about his wound which was being treated with scarlet red. On the twenty-sixth postoperative day his temperature rose to 101.2° F. The spinal fluid cell count increased to 1,362 with a rise in polymorphonucleocytes to 64 percent. The spinal fluid sugar dropped to 18 mg. per 100 cc., and the protein was 183 mg. per 100 cc. Normal spinal fluid dynamics were present. Repeated blood cultures were negative.

On the twenty-ninth postoperative day, cultures of spinal fluids obtained on the twenty-fourth and twenty-sixth postoperative days were reported as showing a growth of *Ps. aeruginosa*. Sensitivity studies indicated a high degree of resistance to the readily available antibiotics, including terramycin, which was then being used, and streptomycin. The diagnosis of pseudomonas meningitis appeared to be clear, but

therapy still remained a problem. No polymyxin was available. The dose of terramycin was increased to 3 grams by mouth and 2 grams intravenously daily. On this dosage there was a fall in the spinal fluid cell count to 688 and a rise in the sugar to 32 mg. per 100 cc. but the fluid remained turbid and under increased pressure. Smears and cultures were negative. Clinically, the patient continued to do well except for intermittent nausea and vomiting.

On the thirty-fifth postoperative day he suddenly became worse. His temperature rose to 102° F. Headache, stiffness of the neck, and vomiting returned. A lumbar puncture revealed elevated pressure. The spinal fluid was turbid and for the first time had a green tinge. The cell count was 8,155 with 82 percent polymorphonucleocytes. The sugar was 20 mg. per 100 cc. and the protein was 357 mg. per 100 cc. It was decided to continue treatment with terramycin, increasing the dose to 6 grams daily by a continuous intravenous infusion containing 1 gram per 500 cc. of fluids. On the following day (the thirty-sixth postoperative day) the patient was improved. His temperature was normal and nuchal rigidity was less. His spinal fluid was still under increased pressure, turbid, and green-tinged. Sufficient fluid was withdrawn to reduce the initial pressure of 385 mm. to 100 mm. By the thirty-eighth postoperative day (the third day of the increased terramycin dosage) his spinal fluid cell count was down to 277 and the sugar was up to 55 mg. per 100 cc.

During the next few days his temperature remained normal. His only symptoms were persistent nausea and vomiting which were attributed to the terramycin. His spinal fluid cell count decreased to 53 on the fortieth postoperative day but the fluid was still green-tinged. Spinal fluid cultures remained negative. The wound of the left buttock had been slowly and steadily diminishing in size, measuring 8 by 3 cm. on the thirty-ninth postoperative day. It was necessary to cannulate veins because of phlebitis resulting from the continuous intravenous use of terramycin. Because the right arm and leg developed marked phlebitis, the concentration of terramycin was decreased to 750 mg. in 500 cc. of fluid on the forty-third postoperative day, the daily dose remaining 6 grams. The patient remained afebrile. His nausea and vomiting persisted. His spinal fluid continued to improve. By the forty-sixth day the fluid was faintly yellow with a cell count of 91 (all lymphocytes). The spinal fluid sugar was 50 mg. per 100 cc. and the protein, 100 mg. per 100 cc. The initial pressure was still elevated. Physical examination was negative except for a pulse rate of 100, the phlebitis, and the healing wound. By the end of the seventh postoperative week, the patient developed a phlebitis with thrombosis of the left antecubital vein.

On the forty-eighth postoperative day (3 weeks after the last positive spinal fluid culture and 2 weeks after starting a daily

intravenous dosage of 6 grams of terramycin) antibiotic therapy was discontinued. At that time the spinal fluid was only faintly yellow with a cell count of 54 (all lymphocytes); the sugar was 65 mg. per 100 cc.; and the protein was 107 mg. per 100 cc. When the terramycin was discontinued, there was a striking disappearance of nausea and vomiting and a return of the appetite. The temperature remained normal. Physical examination on the forty-ninth postoperative day revealed a pulse of 120, subsiding phlebitis of 3 extremities, and a wound of the left buttock measuring only 6 by 1.5 cm. Because of the tachycardia, an ECG was taken. Serial lumbar punctures were continued and the spinal fluid showed steady improvement.

One week after the treatment with terramycin was stopped, the patient noted mild early morning headaches for several days. On the fifty-sixth postoperative day his temperature rose to 102° F. and he had 2 watery stools without abdominal pain. On the following day his rectal temperature was 99.8° F. Examination revealed a pulse of 100 and almost complete disappearance of the phlebitis of his right arm and right leg but persistent phlebitis with thrombosis of his left antecubital vein. His wound measured 4 by 0.5 cm. Muscular atrophy and weakness of his legs was marked. A lumbar puncture yielded crystal-clear fluid under a pressure of 250 mm. The spinal fluid cell count was 60 (all lymphocytes); the protein was 82 mg. per 100 cc.; and the sugar was 45 mg. per 100 cc. His temperature quickly fell to normal and he again became asymptomatic. He continued to do well thereafter. His wound was completely healed by the seventy-second postoperative day. His course after the treatment with terramycin was discontinued indicated that a satisfactory response of the meningitis to the therapy had been achieved.

A new problem was encountered, however. Toward the end of the course of intensive terramycin therapy, a persistent tachycardia was noted. An ECG, taken on the day following cessation of the treatment with terramycin, revealed low T waves in the standard limb leads and inversion of T waves in leads V_1, V_2, V_3, and V_4. This was a change from an ECG taken on the nineteenth postoperative day, prior to intensive intravenous treatment with terramycin, which showed upright T waves (except in lead V_1). Apart from the persistent tachycardia and the T-wave changes, no cardiac abnormality was detected. Serial ECG's showed partial return of the T waves to normal by the fifty-third postoperative day and complete return by the sixty-first postoperative day, 13 days after the treatment with terramycin was stopped. The electrocardiographic findings remained normal thereafter. The pulse rate remained elevated even after return of the T waves to normal.

On the seventy-second postoperative day slow ambulation and mild physical therapy for the loss of muscle strength and substance were started. The patient remained afebrile and asymptomatic. His pulse rate slowly returned to normal. His sedimentation rate continued to be elevated. His spinal fluid remained clear, showing on the eightieth postoperative day slightly elevated pressure, moderate pleocytosis (24 lymphocytes), and elevation of the protein content (96 mg. per 100 cc.). Satisfactory progress was maintained until the ninety-second postoperative day, 6 weeks after treatment was stopped, when he developed a pleuritic pain in the left upper anterior portion of his chest. A roentgenogram of his chest revealed a small area of increased density in the second left anterior interspace. During the next few days, this cleared completely and he again became asymptomatic. His pulse rate remained normal, his sedimentation rate returned to normal, and by the start of his fourth postoperative month he was fully ambulatory, afebrile, and asymptomatic.

DISCUSSION

This case is of interest for 3 reasons. *First,* meningitis due to *Ps. aeruginosa* was successfully treated with large intravenous doses of terramycin. Although minimal pleocytosis and elevated protein were still present in the spinal fluid 1 month after treatment was stopped, the negative cultures and the afebrile, asymptomatic clinical course leave no doubt that the infection had been eradicated. This suggests that large doses of terramycin are useful in the treatment of such infections. The intravenous use of terramycin may not be without hazard, but it will extend the available armamentarium.

The *second* point of interest is the information obtained concerning the administration of varying concentrations and dosages of terramycin given intravenously. Because of the nausea and vomiting, terramycin could not be given by mouth. With the dosage initially used, there was some immediate improvement, but then a balance seemed to result between the infection and the terramycin. Sensitivity studies revealed marked resistance of the organisms to terramycin in vitro. With the sudden change in the patient's condition on the thirty-fifth postoperative day, it became necessary to try a different therapeutic approach. Because polymyxin was not available, it was decided to exceed what had been considered a safe dosage and increase the amount of terramycin given to 6 grams intravenously each day. Fortunately this was successful and no serious evidences of toxicity developed. In daily doses of 1 or 2 grams in 1 or 2 liters of fluid respectively, no difficulty in the administration of terramycin was encountered over a 25-day period, but when a continuous intravenous infusion of 3 liters per day containing 2

grams of terramycin per liter was given, phlebitis rapidly developed. When the concentration was reduced to 1.5 grams per liter and 4 liters were given per day, the development of phlebitis was markedly slowed. Throughout the entire course, nausea, anorexia, and vomiting accompanied the intravenous use of terramycin. When treatment was stopped, these symptoms promptly disappeared.

The *third* point of interest is the development of a persistent tachycardia and T-wave changes during intensive intravenous terramycin therapy. These slowly subsided. Whether the tachycardia and T-wave changes were part of the course of the disease or were caused by the terramycin therapy cannot be stated.

EDITOR'S NOTE: On page 194 of Annals of Internal Medicine, July 1952, Ginsberg, I. A., and Hyman, G. A., report the successful treatment of a patient with *Ps. aeroginosa* meningitis with combined aureomycin and streptomycin; and on pages 1395-1397 of the Journal of the American Medical Association, Aug. 9, 1952, Knight, V.; Hardy, R. C.; and Negrin, J., Jr., report the successful intrathecal use of streptokinase and streptodornase and intramuscular and intrathecal use of neomycin in meningitis due to *Ps. aeruginosa.*

BOOKS RECEIVED

Intracranial Aneurysms, by *Wallace B. Hamby,* M. D., Professor of Neurological Surgery, The University of Buffalo School of Medicine and Dentistry, Buffalo General Hospital, Buffalo, N. Y. 564 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $14.25.

Brain Mechanisms in Coronary Disease, Causation, Treatment, and Prevention, by *N. E. Ischlondsky,* M. D., Author of Brain and Behaviour; Protoformotherapy in Treatment and Prevention; Der Bedingte Reflex und Seine Bedeutung; Physiologische Grundlagen der Tiefenpsychologie, etc. With Two Appendices: 1. From the Conditioned Reflex to the Science of Brain Dynamics. Paper delivered at the XVIIIth International Congress of Physiology. 2. Reflexologic Bases of Personality. Paper delivered at the Ninety-Sixth Annual Meeting of the American Psychiatric Association. 171 pages; illustrated. Henry Kimpton, London, England, publisher, 1952.

Applied Physiology, by *Samson Wright,* M. D., F. R. C. P., John Astor Professor of Physiology, University of London, Middlesex Hospital Medical School; Sometime Examiner in Physiology to the Universities of Oxford, London and Leeds; the Royal College of Surgeons of England; the Royal College of Surgeons of Edinburgh; the Conjoint Board in England; the Conjoint Board in Ireland, with the collaboration of *Montague Maizels,* M. D., F. R. C. P., Professor of Clinical Pathology, University of London, University College Hospital Medical School, and *John B. Jepson,* M. A., B. Sc., D. Phil., A. R. I. C., Senior Lecturer in Biochemistry, Courtauld Institute of Biochemistry, Middlesex Hospital Medical School. 9th edition. 1,190 pages; illustrated. Geoffrey Cumberlege Oxford University Press, New York, N. Y., publisher, 1952.

Claude Bernard and the Experimental Method in Medicine, by *J. M. D. Olmsted,* Professor of Physiology at the University of California; Membre correspondant de la Société philomathique de Paris. Prix Binoux, Académie des Sciences, 1949, and *E. Harris Olmsted.* 277 pages. Henry Schuman, Inc., Publisher, New York, N. Y., 1952. Price $4.

Physical Foundations of Radiology, by *Otto Glasser,* Professor of Biophysics and head of Department of Biophysics, Cleveland Clinic, Foundation, Cleveland, Ohio; *Edith H. Quimby,* Associate Professor of Radiology (Physics), College of Physicians and Surgeons, Columbia University, New York; *Lauriston S. Taylor,* Chief, Atomic and Radiation Physics Division, National Bureau of Standards, Washington, D. C.; *J. L. Weatherwax,* American Oncologic Hospital and Graduate School of Medicine, University of Pennsylvania, Philadelphia. 2d edition, revised and enlarged. 581 pages; illustrated. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1952. Price $6.50.

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Pictorial Handbook of Fracture Treatment, by *Edward L. Compere,* M. D., F. A. C. S., Associate Professor of Surgery, Northwestern University Medical School; Chairman, Departments of Orthopedic Surgery, Wesley Memorial and Children's Memorial Hospitals; Consultant in Orthopedics, Chicago Memorial and Henrotin Hospitals; Medical Adviser and Director, Rehabilitation Center of the Liberty Mutual Insurance Company, Chicago, and *Sam W. Banks,* M. D., F. A. C. S., Associate Professor in Surgery, Northwestern University Medical School; Attending Orthopedic Surgeon, Chicago Memorial, Woodlawn and Hines Veterans Hospitals, Chicago. Revised with the assistance of *Clinton L. Compere,* M. D., F. A. C. S., Assistant Professor of Surgery, Northwestern University Medical School; Attending Orthopedic Surgeon, Wesley Memorial Hospital; Consultant in Orthopedic Surgery, Augustana Hospital; Senior Consultant, Veterans Administration, Chicago. 424 pages; illustrated. The Year Book Publishers, Inc.. Chicago, Ill., 1952. Price $6.50.

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HISTOCHEMICAL DETECTION OF FATAL ANTICHOLINESTERASE POISONING

A. DOROTHY BERGNER, *Ph. D.*

MILWARD W. BAYLISS, *Colonel, MC, U. S. A.* (1)

THERE has been a recent increase in the use of chemicals which act as cholinesterase (ChE) inhibitors. These anticholinesterases include therapeutic agents, such as those used in the treatment of myasthenia gravis (2-7) and certain insecticides. In cases of poisoning by such agents, the clinical syndrome is well defined and, in general, similar to acetylcholine intoxication (3-6, 8-10). On the other hand, at necropsy the findings are nonspecific and consist only of pulmonary and cerebral edema accompanied by petechial hemorrhages in the serous membranes and viscera. Ordinary toxicologic procedures cannot be relied on because the amount of toxic material absorbed in fatal cases is small and because the compounds tend to hydrolyze in the body fluids.

(1) From the Chemical Corps Medical Laboratories, Army Chemical Center, Md.

(2) Schlezinger, N. S.: Present status of therapy in myasthenia gravis. J. A. M. A. 148: 508-513, Feb. 16, 1952.

(3) Stone, C. T., and Rider, J. A.: Treatment of myasthenia gravis. J. A. M. A. 141: 107-111, Sept. 10, 1949.

(4) Comroe, J. H., Jr.; Todd, J.; Gammon, G. D.; Leopold, I. H.; Koelle, G. B.; Bodansky, O.; and Gilman, A.: Effect of di-isopropylfluorophosphate (DFP) upon patients with myasthenia gravis. Am. J. M. Sc. 212: 641-651, Dec. 1946.

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(7) Rider, J. A.; Schulman, S.; Richter, R. B.; Moeller, H. C.; and DuBois, K. P.: Treatment of myasthenia gravis with octamethyl pyrophosphoramide; preliminary report. J. A. M. A. 145: 967-972, Mar. 31, 1951.

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(9) Grob, D.; Garlick, W. L.; Merrill, G. G.; and Freimuth, H. C.: Death due to parathion, anticholinesterase insecticide. Ann. Int. Med. 31: 899-904, Nov. 1949.

(10) Grob, D.; Garlick, W. L.; and Harvey, A. M.: Toxic effects in man of anticholinesterase insecticide parathion (p-nitrophenyl diethyl thionophosphate). Bull. Johns Hopkins Hosp. 87: 106-129, Aug. 1950.

In the absence of reliable pathologic or toxicologic procedures, some method is needed for determining the cause of death in cases of suspected anticholinesterase poisoning. Such a method must depend on demonstration by either a manometric or histochemical technic of inhibition of the enzyme, ChE, in the postmortem material. In reports of fatal parathion poisoning, manometric determinations of ChE activity in blood and tissues removed at necropsy have been reported *(9, 10)*.

That a histochemical method also is available was indicated recently *(11)*. As a result of experiments using mouse and human tissue removed at necropsy, it was shown that a histochemical method for the demonstration of active ChE in tissues can be applied to postmortem material for the detection of acute anticholinesterase poisoning. The method followed was the histochemical technic of Koelle and Friedenwald for localizing ChE activity in teased or frozen sections of unfixed tissues *(12, 13)*.

Cholinesterases are enzymes which hydrolyze carboxylic acid esters of choline. Koelle and Friedenwald used acetylthiocholine as a substrate because it is hydrolyzed more rapidly than acetylcholine by both specific and nonspecific esterases. In their method acetylthiocholine is hydrolyzed in the presence of copper glycinate. Copper thiocholine is formed at the site of enzymatic action. This white precipitate reacts with dilute ammonium sulfide to produce dark brown copper sulfide which is easily visible. The chemical reactions are:

Reaction 1.

$$2\ CH_3COSCH_2CH_2N(CH_3)_3OH + (NH_2CH_2COO)_2Cu + 2\ H_2O + ChE \longrightarrow$$

(acetylthiocholine) (copper glycinate) (enzyme)

$$Cu(SCH_2CH_2N(CH_3)_3OH)_2 + 2\ NH_2CH_2COOH + 2\ CH_3COOH$$

(copper thiocholine) (glycine) (acetic acid)

Reaction 2.

$$Cu(SCH_2CH_2N(CH_3)_3OH)_2 + (NH_4)_2S \longrightarrow CuS + 2\ NH_4SCH_2CH_2N(CH_3)_3OH$$

(copper thiocholine) (ammonium sulfide) (copper sulfide) (ammonium thiocholine)

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(11) Bergner, A. D., and Durlacher, S. H.: Histochemical detection of fatal anticholinesterase poisoning. Am. J. Path. 27: 1011-1021, Nov.-Dec. 1951.

(12) Koelle, G. B., and Friedenwald, J. S.: Histochemical method for localizing cholinesterase activity. Proc. Soc. Exper. Biol. & Med. 70: 617-622, Apr. 1949.

(13) Koelle, G. B.: Histochemical differentiation of types of cholinesterases and their localizations in tissues of cat. J. Pharmacol. & Exper. Therap. 100: 158-179, Oct. 1950.

Because possible diffusion of the copper thiocholine is kept at a minimum, if not entirely suppressed, the presence of a deposit of CuS indicates a site of ChE activity. In striated muscle the site of the motor end plate is clearly differentiated from the muscle fiber, as shown in figure 1. When enzymatic action is inhibited, there is no deposit at the site. Without such a deposit the motor end plate cannot be distinguished from the muscle fiber.

MODIFICATION OF TECHNIC

The procedure followed in adapting the Koelle-Friedenwald technic for use in cases of fatal poisoning was dictated by the nature of the problem, namely, the need for a simple method which could be applied to postmortem material. Preliminary runs with biopsy specimens showed that the method was reasonably simple to perform and gave reproducible results on repetition.

The method was simplified by limiting the choice of tissue to striated muscle. This muscle is easy to obtain and, if the sample contains fibers an inch long for human material (shorter for smaller animals, depending on their size), should include some motor end plates. A further advantage lies in the fact that these fibers can be teased apart easily and are easy to handle during the test for ChE activity. The necessity of making frozen sections of unfixed tissues is avoided. Thus the advantages of testing unfixed material are retained but the danger of adsorption artefacts is avoided. Advantage was also taken of the fact that in striated muscle the ChE present is mostly of the specific type and is located at the motor end plate. That it is firmly attached to this structure is shown by the fact that even after muscle has been washed repeatedly in saline solution, much ChE activity remains. Moreover it is present in great concentration at this site; particularly in the subneural apparatus.

These facts permit further simplification of the technic. Because only one type of ChE is present in measurable amount, it is necessary to test with only one substrate. Localization of specific ChE is favored over that of nonspecific ChE by maintenance of the substrate concentration (4×10^{-3}M) in the optimal range for the specific type. Also, because there is a concentration of enzyme at the motor end plate, a mass of CuS is normally deposited at this site (fig. 1). Consequently it is easier to distinguish between the normal amount and any reduction in intensity or area of the deposit. A reduced amount of CuS is a consequence of partial inhibition of enzymatic activity (fig. 2) and absence of deposit, of complete inhibition (fig. 3). Thus the technic can be used for a quasi-quantitative estimate of ChE activity or inhibition at the motor end plates.

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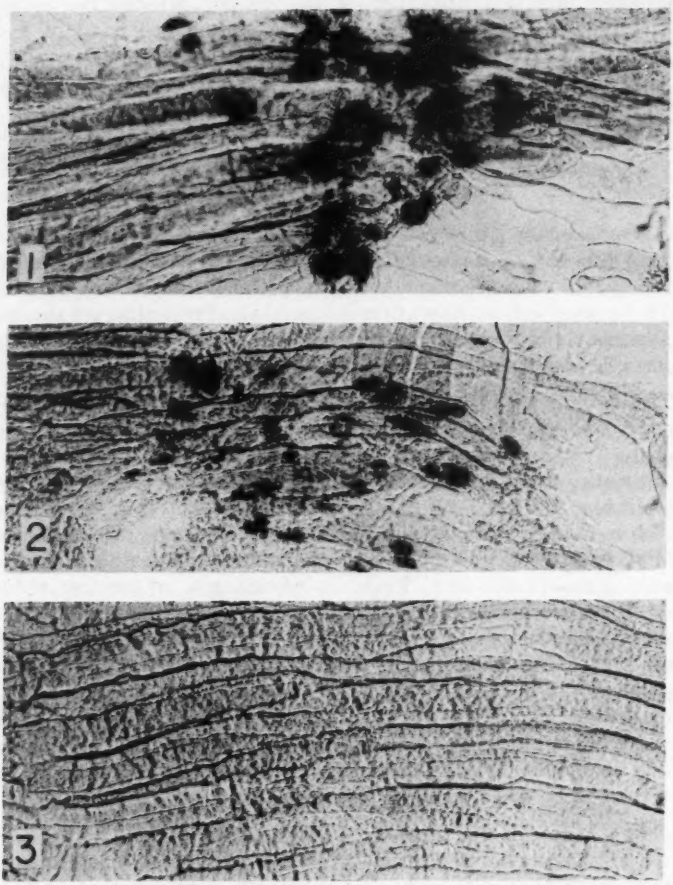

Figure 1. X 77. Intercostal muscle from mouse sacrificed with pentobarbital sodium and necropsied immediately. Typical dark deposit of CuS may be seen at the site of the motor end-plates, indicative of uninhibited ChE activity. Figure 2. X 77. Intercostal muscle from mouse sacrificed with TEPP and necropsied after 24 hours at room temperature. Moderate deposit of CuS indicative of partial inhibition of ChE activity may be seen. Figure 3. X 77. Intercostal muscle from mouse sacrificed with DFP and necropsied immediately. No CuS was deposited at motor end-plate, indicating complete inhibition of ChE activity.

MATERIAL

Reagent 1 consists of 1.88 grams of glycine, 2 ml. of normal KOH, and distilled water to make 50 ml.

Reagent 2 consists of 0.1 M copper sulfate solution.

Reagent 3 consists of 0.2 M KH_2PO_4.

Reagent 4 consists of 0.2 M Na_2HPO_4.

Reagent 5 consists of 15 mg. of acetylthiocholine iodide *(14)*, 0.75 ml. of water, and 0.25 ml. of reagent 2. This is centrifuged and the supernatant solution is decanted from the precipitate.

Reagent 6 (copper thiocholine) consists of 29 mg. of acetylthiocholine iodide, 1 ml. of water, and 0.6 ml. of reagent 2. This is centrifuged and filtered. To the filtrate and two 1 ml. washings 1 ml. each of reagents 1 and 2 are added, then normal KOH is added until the pH is between 9 and 10. This is allowed to stand at room temperature until precipitation is complete; this requires several hours. The precipitate is collected by centrifugation and washed twice with small amounts of water.

Reagent 7 consists of ammonium sulfide, C. P. Immediately before use this is diluted 1:18 and saturated with CuS by adding a drop of reagent 2. It is then centrifuged and the supernatant solution is decanted from the precipitate.

Reagents 1, 3, and 4 are kept under refrigeration.

The *incubation solution* consists of 3.8 ml. of water, 0.2 ml. of reagent 1, 0.2 ml. of reagent 2, 3.5 ml. of reagent 3, and 1.5 ml. of reagent 4. It is saturated with reagent 6 and incubated at 37° C. for 15 minutes. Immediately before using 0.9 ml. of reagent 5 is added. It is filtered and used at once.

The *rinse solution* consists of 4.8 ml. of water, 0.2 ml. of reagent 1, 4 ml. of reagent 3, and 1 ml. of reagent 4. This is saturated with reagent 6 and centrifuged. The supernatant solution is decanted from any precipitate.

The *final solution* consists of distilled water saturated with CuS.

METHOD

Striated muscle obtained at necropsy is frozen as quickly as possible and kept frozen until it is tested histochemically. While solutions needed for the test are being prepared, the muscle to be tested is removed from the cold. As soon as there has been sufficient thawing, a suitable portion is selected and teased apart in isotonic (0.9 percent) saline solution at room temperature, placed at once in freshly prepared incubation solution and incubated at 37° C. The bits of teased muscle are transferred to the rinse solution and agitated for 1 or 2 minutes. They are then

(14) Acetylthiocholine iodide can be obtained from LaWall and Harrisson, 1921 Walnut Street, Philadelphia, Pa.

immersed in reagent 7 for 30 seconds only and transferred to the final solution where they may remain until they are mounted in glycerin on a glass slide and covered by a coverglass. On the following day the coverglass is ringed with mastic-paraffin. Syracuse dishes and glass needles are used. The teasing of the muscle and the selection of the tested fibers for mounting in glycerin are done with the aid of a dissecting microscope at a magnification of x 10.

Teased striated muscle from a control animal of the same species is always tested with the same incubation solution that is used for testing muscle from the poisoned animal. This is done either by dividing the freshly prepared incubation solution into 2 portions, using 1 portion for each sample of tissue, or by using the solution a second time, after it has been filtered, to test the control tissue. The purpose in using the same solution for both samples of tissues is to check the strength of the solution and to determine the normal amount of CuS deposit. Using this deposit as a standard, it is then possible to make a comparison with the deposit in the poisoned animal.

In order to have control tissue of the various species available when needed, tissue is stored at from -40° to -50° C. It has been kept at this temperature without any loss of enzymatic activity for periods of more than 6 months. Intercostal muscle is recommended if a choice is possible. Adequate penetration of substrate to the sites of the enzyme in the tissues is most essential. Therefore a primary bundle should be teased apart into fine strands of fibers to afford maximum exposure of motor end plates to the substrate in the incubation solution. For this same reason, the dish should be agitated occasionally during incubation. The length of this incubation period varies with the species. For example, 15 minutes is satisfactory for a small rodent; 25 minutes for a cat, dog, or monkey; 25 or 30 minutes for a goat, mule, or man.

APPLICATION OF TECHNIC TO POSTMORTEM TISSUE

By way of illustrating the usefulness of this technic, brief reference will be made to experiments reported by Bergner and Durlacher *(11)*

Stability of ChE in postmortem material. It was necessary to determine the stability of ChE in postmortem material because necropsy is usually not performed immediately after death. Mouse and human muscle was used. Mice sacrificed by fracture of the neck were kept at room temperature (20° to 26° C.) and examined at varying intervals after death. At necropsy, intercostal muscle was removed and frozen. When tested histochemically such muscle showed that there had been little decrease in ChE activity at the motor end plate for as long as 48 hours after death although

severe portmortem putrefaction was present. Intercostal muscle removed from human cadavers as soon as possible after death and from cadavers undergoing postmortem decomposition also was examined. When tested, such muscle showed that ChE activity persisted post mortem in human intercostal muscle for at least 26 hours at 20° to 26° C. and in refrigerated bodies for as long as 180 hours.

In vitro poisoning of human postmortem material. It is possible to use postmortem material to demonstrate in vitro poisoning by anticholinesterases. Human striated muscle was removed at necropsy from 2 cadavers in whom the manner of death was a bullet wound of the head and a gunshot wound of the chest, respectively. Muscle was incubated in saline solutions containing DFP, rinsed in saline solution, and subjected to the histochemical technic. Comparison was made with fragments of the muscle that had not been incubated with DFP. Incubation for 10 minutes in 1×10^{-4} percent of DFP caused complete inhibition of ChE activity (no CuS deposit). When the dilution was 1×10^{-5} percent of DFP, a faint deposit of CuS at the site of the motor end plate was observed indicating a marked reduction in ChE activity.

Distinction between deaths caused by anticholinesterases and by other poisons. In order to learn whether this method could be used to distinguish between poisons which are anticholinesterases and those which are not, mice were fatally poisoned by various agents. Half of the animals were examined immediately after death and the other half after 24 hours. At necropsy intercostal muscle was removed and frozen. Later it was tested histochemically. By evaluating the amount of CuS at the site of the motor end plate, the intensity of ChE activity could be estimated.

Mice were fatally poisoned by various chemicals known to be lacking in anticholinesterase activity and including those commonly associated with accidental or suicidal deaths among human beings. They were ether, illuminating gas containing carbon monoxide, potassium cyanide, sodium arsenite, morphine sulfate, pentobarbital sodium, BAL, acetylcholine chloride, ANTU, and sodium monofluoracetate. The doses administered caused death in 30 minutes or less except following morphine, ANTU, and sodium monofluoracetate. In no instance was any diminution of ChE activity noted either when necropsy was performed immediately after death or when it was delayed for 24 hours.

Mice were fatally poisoned also by several of the better known anticholinesterases. They were DFP, physostigmine, neostigmine, parathion, TEPP, and OMPA. The doses were large enough

to cause death in less than 1 hour. In tissues taken from these animals there was diminished deposition if not complete absence of CuS. This altered deposition indicated partial or complete enzyme inhibition. Even when the deposit was increased as a result of delay in necropsy following death from a temporary inactivator such as physostigmine, the CuS deposit was sufficiently reduced to be distinct from that in normal tissue or even in tissue from animals fatally poisoned by noncholinesterase-inhibiting agents. These facts indicate that this method can be used in suspected poisoning of human beings by ChE inhibitors.

BOOK REVIEWS

The Pathogenesis and Treatment of Thrombosis, With a Clinical and Laboratory Guide to Anticoagulant Therapy, by *Irving S. Wright,* M. D., Professor of Clinical Medicine, Cornell University Medical College, New York. Modern Medical Monographs, No. 1. 78 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., publisher, 1952. Price $3.

In this book the author offers a partial explanation for the complex mechanism of blood clotting on a physicochemical basis. He does not expect the theory to revolutionize the older concepts but rather augment them and to offer a new approach to an old and difficult problem. A portion of the monograph is devoted to therapy and brief descriptions of laboratory procedures. The text is easy to read, brief, and informative.

—*Capt. L. H. Thomas, MC, U. S. A.*

Rheumatic Diseases, Based on the Proceedings of the Seventh International Congress on Rheumatic Diseases. Prepared by *The Committee on Publications of The American Rheumatism Association. Charles H. Slocumb,* M. D., Chairman. *Howard F. Polley,* M. D., *William D. Robinson,* M. D., *Richard T. Smith,* M. D., *Charles Ragan,* M. D., *Edward F. Rosenberg,* M. D., and *Carlos Sacasa,* M. D. 449 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publisher, 1952.

The contributors to this book are outstanding in the field of rheumatic diseases. The discussion of all the rheumatic diseases is comprehensive and includes investigative, clinical, and therapeutic aspects. The many illustrations enhance the book's value. The discussion of our current knowledge of the effects of endocrine secretions on articular tissues is of special interest. This book covers the field of rheumatic diseases so thoroughly that any one can by reading it be brought up to date on all phases of the subject without resorting to an exhaustive search of the literature.—*Col. D. J. Waligora, MC, U. S. A.*

LIDOCAINE IN DENTISTRY[1]

DOUGLAS C. WENDT, *Major, U. S. A. F. (DC)*

THIS report is based on a study of over 300 patients on whom lidocaine was used. Procaine hydrochloride is highly acceptable as an anesthetic agent and it has become the most widely used local anesthetic in dentistry. Despite the universal acceptance of procaine, a more rapidly acting agent which is capable of producing a more intense anesthesia is often desirable. After the American Dental Association accepted lidocaine as a local anesthetic in the fall of 1950, I started using this drug in routine dental practice and compared its effectiveness with that of 2 percent procaine.

Three different solutions were used: 2 percent lidocaine with 1:50,000 epinephrine; 2 percent lidocaine with 1:100,000 epinephrine; and 2 percent lidocaine without epinephrine. The drug was administered in carpule form, using a standard carpule syringe. It was used for routine dental procedures on patients who presented themselves for treatment in the dental clinic. The following data was recorded for each case: type of anesthesia and amount of epinephrine, quantity used, type of injection, time administered, length of anesthesia, and any reactions or symptoms noted.

Early observations indicated that effective operative anesthesia was obtained rapidly after its administration. With infiltrative injections anesthesia occurred, in many instances, shortly after the needle was withdrawn. Table 1 shows the range of the onset of anesthesia for the 3 solutions used in infiltrative and conductive injections.

The rapid action of lidocaine was a timesaving factor because patients were usually ready for operation in less than 3 minutes. In the few instances where the anesthesia was incomplete, the patient gave a history of lack of confidence in local anesthetics. The rapid action of the drug may be due to its high degree of diffusibility. In infiltrative injections it diffuses more readily than procaine. This usually makes additional injections for adjacent teeth unnecessary. Its diffusion over a larger area also reduces the number of unsuccessful injections. I have found the injection of lidocaine into the mental foramen to be more effective than procaine.

(1) Headquarters, Military Air Transport Service, Andrews Air Force Base, Washington, D. C.

The profoundness of lidocaine anesthesia is one of its most noteworthy attributes. In the field of oral surgery 2 percent lidocaine with epinephrine 1:50,000 is preferable for such procedures as impactions and multiple extractions. It provides a deep and lasting anesthesia. In single extractions and alveolectomies 2 percent lidocaine with epinephrine 1:100,000 was most effective. Two percent lidocaine without epinephrine was less effective but proved valuable in the uncomplicated extraction of maxillary third molars. In the operative and crown and bridgework, it also proved to be a valuable anesthetic agent. In patients whose teeth required extensive tooth preparations, 2 percent lidocaine with epinephrine 1:50,000 or 1:100,000 proved most satisfactory.

TABLE 1. *Time required for effective anesthesia (minutes)*

Anesthetic	Infiltrative			Conductive		
	Minimum	Maximum	Average	Minimum	Maximum	Average
2 percent lidocaine with epinephrine 1:50,000	0.0	6.0	1.8	0.5	8.0	2.21
2 percent lidocaine with epinephrine 1:100,000	0.0	3.0	1.37	0.0	7.0	1.57
2 percent lidocaine without epinephrine	0.5	6.0	2.18	1.0	6.0	2.58
2 percent procaine with epinephrine 1:50,000	2.0	10.0	4.0	2.0	9.0	4.2

Lidocaine produced complete anesthesia in many patients in whom procaine previously had not been effective. An interesting example was a patient for whom three-quarter crown preparations for a bridge were to be constructed on the maxillary left central incisor and the maxillary right lateral incisor. Two percent procaine was administered and the proximal slices were made when the signs of anesthesia were apparent. The patient complained that the anesthesia was incomplete and after a second injection of 2 percent procaine was given with the same results, he was dismissed. Later 2 percent lidocaine with epinephrine 1:50,000 was administered in the same manner and the operation was completed painlessly. Many similar cases could be cited.

In periodontia, extensive gingivectomies were performed using lidocaine as the anesthetic. Satisfactory anesthesia was also obtained using lidocaine with epinephrine 1:100,000 and

lidocaine with epinephrine 1:50,000. Root canal therapy on vital pulps was accomplished using lidocaine and excellent anesthesia was obtained in all cases. Although lidocaine without epinephrine was the least satisfactory of the three solutions used, it proved effective for simple operations and for patients in whom the use of epinephrine was contraindicated.

The duration of effective anesthesia is important. Lidocaine provided anesthesia of sufficient duration (table 2). It was noted that a long-acting anesthetic agent was not only effective in complicated oral operations, but was also effective in eliminating much of the immediate postoperative distress and pain. This gives the added advantage of allowing time for the patient to relax and for a clot to form.

TABLE 2. *Duration of anesthesia (minutes)*

Anesthetic	Infiltrative			Conductive		
	Minimum	Maximum	Average	Minimum	Maximum	Average
2 percent lidocaine with epinephrine 1:50,000	80	270	159	90	398	184
2 percent lidocaine with epinephrine 1:100,000	65	294	151	100	255	164
2 percent lidocaine without epinephrine	14	188	87	14	165	104
2 percent procaine with epinephrine 1:50,000	37	108	67	43	112	73

Although occasional side reactions and postoperative reactions occur in the use of most local anesthetics, none were noted with lidocaine in this series. In 2 patients who repeatedly developed headaches after injections with procaine, lidocaine was used several times without inducing headache. These patients were given the anesthetic in the same manner and were unaware that a different drug was being used.

In most patients 1 cc. of solution was effective for infiltrative injections and 1.8 cc. for conductive injections. Although injections of lidocaine were only half the size of those of procaine it was found to be just as effective. The smaller quantity of solution has the advantage that it causes less distention of the tissues. It was noted that when the anesthesia wore off, it did so as rapidly as the onset appeared. There were also less distressing effects such as burning, tingling, or paresthesia when lidocaine was used.

CONCLUSIONS

Lidocaine acts much more rapidly than procaine and produces a deeper anesthesia, particularly in patients in whom anesthesia is difficult to induce. In our patients it produced no noteworthy side effects or postoperative reactions. The diffusibility of lidocaine increases the effectiveness of infiltrative injections and injections of the mental foramen.

BOOK REVIEW

Korea, 1950. *Office of the Chief of Military History, Department of the Army.* 281 pages; illustrated. Government Printing Office, Washington, D. C., publisher, 1952. Price $1.25.

This book, written by one of the most distinguished military authors, follows the principle that one picture is worth a thousand words. The text is built around a group of carefully selected photographs which depict military operations of the Armed Forces in Korea from the beginning of the invasion of South Korea by the Communist forces of North Korea on 25 June 1950 to 31 December 1950, when the troops of the United States and other United Nations forces were regrouped south of the thirty-eighth parallel for a new drive toward the north. This condensed history includes graphically and descriptively, every major type of military operation known in history.

The early fighting withdrawal to the perimeter defense of Pusan was followed by the amphibious Inchon landing and the counter offensive and break-out from the Pusan perimeter. The classic pursuit and annihilation of the North Korean Communist forces is depicted in the dash for the Yalu River. The entry of the Chinese Communist forces initiated a second withdrawal of the United Nations forces through a succession of delaying positions in the west, and a withdrawal from the beach at Hamhung. The cycle was completed with the establishment of defensive positions south of the Han River where the forces regrouped for a new counteroffensive.

Incidental to this graphic presentation of a series of different types of military operations is the transition from the heat of the summer to the extreme cold of a winter campaign. A brief and condensed prelude to the entire series of military operations clarifies for the reader the historical events which preceded and led to the invasion of South Korea.

—Brig. Gen. C. F. Sams, MC, U. S. A.

DESMOID TUMOR OF THE SACROSPINALIS MUSCLE[1]

BEVERLY H. WHITE, M. D.

JOSEPH M. MILLER, M. D. [2]

DESMOID tumors are rare, unencapsulated, infiltrating fibromas that usually arise from the musculoaponeurotic structures of the anterior abdominal wall. Their occurrence in other muscle groups is about half as frequent as in this location (3). They differ from other fibromas in that they are larger, more deeply situated, infiltrate and destroy muscle tissue, tend to recur following surgical removal, and occasionally exhibit foci of sarcomatous degeneration (4-7). Instances of distant metastases or involvement of the regional lymph nodes have not been reported, but the tumors may become locally inoperable because of massive infiltration of adjacent structures (5, 8, 9). Most instances of malignant degeneration have occurred in men (5). Pfeiffer (7) noted malignant changes in 10.6 percent of the women and in 24.4 percent of the men in a series of 400 patients. Factors of etiologic significance which have been mentioned are age, sex, pregnancy, and trauma. Most desmomas occur in young parous women (10) and a history of trauma is elicited in a significant percentage of them. Some authors consider trauma to be the most important etiologic factor and believe that most instances occur following pregnancy because of trauma

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(1) Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

(2) Veterans Administration Hospital, Fort Howard, Md.

(3) Pemberton, J. deJ.: Discussion. In footnote reference (4).

(4) Green, C. C.: Desmoid tumor. Arch. Surg. 50: 304-306, June 1945.

(5) Pack, G. T., and Ehrlich, W. E.: Neoplasms of anterior abdominal wall with special consideration of desmoid tumors; experience with 391 cases and collective review of literature. Intemat. Abstr. Surg. 79: 177-198, 1944; in Surg., Gynec. & Obst. Sept. 1944.

(6) Pearman, R. O., and Mayo, C. W.: Desmoid tumors; clinical and pathologic study. Ann. Surg. 115: 114-125, Jan. 1942.

(7) Pfeiffer, C.: Die Desmoide der Bauchdecken und ihre Prognose. Beitr. z. klin. Chir. 44: 334-401, Nov. 1904.

(8) Booher, R. J., and Pack, G. T.: Desmomas of abdominal wall in children. Cancer 4: 1052-1065, Sept. 1951.

(9) Stone, H. B.: Desmoid tumors of abdominal wall. Ann. Surg. 48: 175-185, Aug. 1908.

(10) Geschickter, C. F., and Lewis, D.: Tumors of connective tissue. Am. J. Cancer 25: 630-655, Nov. 1935.

to the anterior abdominal wall during labor. If this be true, it is difficult to explain the rarity of this tumor *(8)*. Congenital desmoid tumors have been reported *(11)*.

In the case to be reported the tumor developed while the patient was in the hospital for treatment of self-induced abscesses. The tumor arose from the right sacrospinalis muscle, a site not previously described.

CASE REPORT

A 35-year-old white woman was admitted to this hospital on 14 May 1947 complaining of recurrent abscesses of the thighs, buttocks, arms, and pectoral regions of 12 years' duration. She had been hospitalized several times elsewhere for treatment, but the cause of the lesions remained obscure. During the period from 1 April 1946 to the time of admission, 31 abscesses, varying from 1 to 5 cm. in diameter, had been incised and drained. Previous hospital records revealed that *Staphylococcus aureus, Proteus vulgaris, Escherichia coli, Escherichia freundii,* alpha micro-aerophilic streptococcus, *Aerobacter aerogenes,* diphtheroids and *Pseudomonas aeruginosa* had been cultured from the abscesses. She had been discharged from the Army in 1944 after 1 year of service with the diagnosis of a severe mixed psychoneurosis.

On admission she was severely emaciated, weighing only 100 pounds, and was unable to stand without assistance. She had a partial fibrous ankylosis of the right knee. Dorsiflexion of both feet was weak. Numerous depressed scars were present over her pectoral regions, buttocks, and upper and lower extremities. Several infected sinus tracts were present on her thighs.

Streptomycin and penicillin therapy was without noticeable effect. New abscesses which developed periodically were aspirated. A diagnosis of constitutional psychopathy and basically unstable personality was made by the consultant in psychiatry. On 14 August the patient was found to possess a syringe and needle and a small bottle containing a feculent-smelling liquid. A culture of this material revealed organisms of the colon group. The patient steadfastly denied having injected the material into herself. Constant surveillance and isolation were instituted, however, with the result that further abscesses did not develop.

On 17 August a small, firm, slightly tender but not inflamed mass was discovered in the right loin just above the iliac crest. At first thought to be an inflammatory process, observation revealed the mass to be a new growth attached to the underly-

(11) Brockman, D. D.: Congenital desmoid of abdominal wall. J. Pediat. 31: 217-219, Aug. 1947.

ing fascia, but not to the skin. A gradual increase in the size of the mass occurred. On 22 October the tumor was excised with a wide margin of normal tissue because of continued enlargement and interference with rehabilitation. At operation the tumor was found to arise from the tendinous portions of the sacrospinalis muscle.

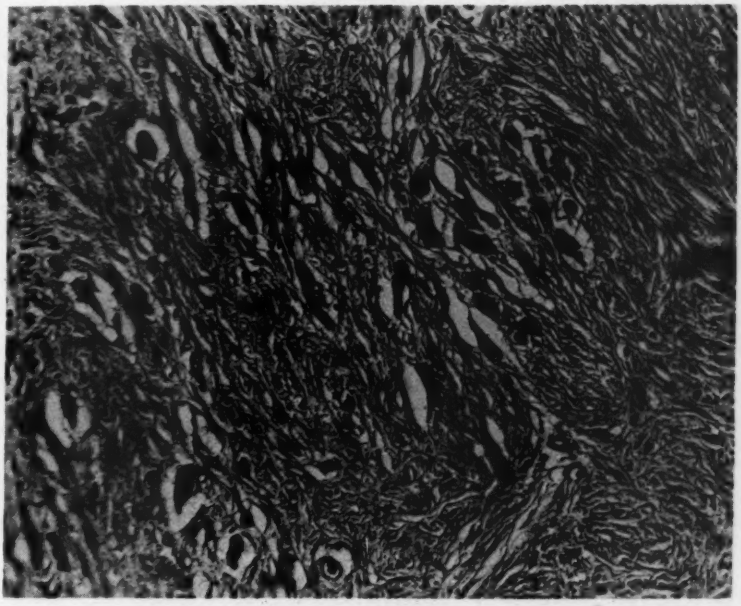

Figure 1. Invasion and encirclement of muscular tissue by the fibrous component of the desmoid tumor.

Gross examination revealed a well-circumscribed nodular tumor measuring 9 by 5 by 4 cm. The cut surface showed a white homogeneous matrix traversed by numerous opaque gray strands which projected slightly above the cut surface. Between the strands were soft gray-white translucent irregular foci. The periphery of the tumor was surrounded by normal muscle.

Microscopically the tumor was composed of uniform stellate fibroblasts separated by numerous interlacing bundles of collagen. Between the nuclei and the poorly defined cytoplasm were numerous interlacing delicate bundles of collagen. In one section the collagen was arranged in parallel, thick bundles resembling the collagen of fascia. Throughout the tumor were nests of atrophied muscle cells (fig. 1). There was infiltration of the surrounding fascia and muscle tissue, but mitotic figures were not observed. A diagnosis of desmoid tumor was made.

The patient's postoperative course was uneventful. At the time of discharge on 3 April 1948 the tumor had not recurred. The patient was given intensive psychotherapy with moderate improvement in her condition, but it was the opinion of the psychiatrist that her basic abnormalities had been helped but little.

SUMMARY

A desmoid tumor was found arising from the sacrospinalis muscle. The diagnosis of the tumor was obscured by numerous self-inflicted abscesses in a constitutionally psychopathic person.

Film Strip Release

The Audio-Visual Production Services of the USPHS Communicable Disease Center has recently released the following productions:

F13a (35 mm., silent, color) Histopathology of Human Fungus Infection. Part I, Superficial Infection (15 frames)

F13b Part II, Cutaneous Infection (16 frames)

F13c Part III, Subcutaneous Infection (17 frames)

F13d Part IV, Systemic Infection (60 frames)

All CDC films are available on free loan for the training of personnel in the fields of public health, medicine, biology, and allied sciences. Inquiries should be directed to: Chief, Audio-Visual Utilization Section, Communicable Disease Center, U. S. Public Health Service, P. O. Box 185, Chamblee, Ga.

THE ESKIMO'S DENTOFACIAL COMPLEX

Effects of Environmental and Genetic Factors

GEORGE V. NEWMAN, *First Lieutenant, DC, U. S. A.*

IN the summer of 1951, I had the opportunity to examine and treat the teeth of Eskimos in Greenland. At the same time I accumulated statistics on the caries, occlusions, and transverse palatal dimensions of these people. A study of environmental (local and nutritional) and hereditary influences on the dentofacial complex of the Eskimos offers the dentist, and particularly the orthodontist, an excellent basis for comparison with that of other races.

About 130 natives reside in the Eskimo village in Thule, northwest Greenland. A small trading station is located in the Danish village (population 40 Danes) about 1 mile away. The original southwest Greenland Eskimo population has become mixed with the white population to a large degree, but in the Thule district the Eskimo element predominates. The last migration of Canadian Eskimos to Greenland, affecting the inbreeding and genetic balance of the Eskimo in the Thule district occurred about 90 years ago.

The range of height of the Eskimo man is from 60 to 65 inches and of the Eskimo woman, from 58 to 60 inches. They are powerfully built with broad chests and short, thick arms and legs. The face of the Eskimo is pentagonal in shape and has a wide bizygomatic and bigonial breadth (figs. 1 and 2). Bimaxillary protrusions are common. The palate is long and broad; a palatal torus is often present. The mandible is heavy and has a high stout body and the ascending rami are broad and low. Mandibular tori are common.

The theories concerning the origin of the Eskimos are numerous and varied, but the most plausible is that of Hrdlicka *(1)* who contended that the Eskimos originally came from northeast Asia across the Bering Strait and that they are derived from an old paleo-Asiatic yellow-brown strain. Pedersen *(2)* also

(1) Hrdlicka, A.: The Coming of Man From Asia in the Light of Recent Discoveries. Annual Report of the Smithsonian Institution, Washington, D. C., 1935. pp. 463-470.

(2) Pedersen, P. O.: The East Greenland Eskimo Dentition-Numerical Variations and Anatomy. C. A. Reitzels Boghandel, Copenhagen, 1949.

concludes on the basis of dental anatomic evidence that the Eskimos are of Mongoloid origin.

NUTRITION AND DENTITION OF THE POLAR ESKIMOS

The modern Eskimo eats a mixed diet. Vegetation is negligible in northwest Greenland. During the winter they eat fish, seal, walrus, polar bear, whales, polar hare, and auks. The meat and fish are eaten raw or semicooked. If the hunting is poor, they may supplement this diet with tea, biscuits, canned foods, and

Figure 1. Modern Eskimo woman (age 27 years). Note canines in labioversion and wide bizygomatic breadth. Figure 2. Primitive Eskimo skull. Note the wide bizygomatic and bigonial breadths.

other items from the nearby Danish trading store. The proportion of carbohydrate in their diet is increased in the summer. Stefansson *(3)* stated that the primitive diet consisting mainly of meat and fish (65 percent protein and 35 percent fat) contains all the minerals and vitamins necessary for (dental) health. Vitamins A, C, and D are found in the glandular viscera of the fatty sea creatures previously mentioned.

The well-developed alveolar processes, the form and size of the jaws, and the lack of observable hypocalcification of the enamel of the teeth confirmed my opinion that there is little, if any, calcium or phosphorus deficiency or disturbance of the calcium-phosphorus ratio during or following the period of tooth formation in these people.

Bertelsen *(4)* and Baarregaard *(5)* pointed out that in 1908 about 10 percent and in 1931 about 50 percent of the food calories were derived from carbohydrate. Furthermore, Bertelsen

(3) Stefansson, V.: Arctic Manual. Macmillan Co., New York, N. Y., 1950. pp. 222-242, 285-288.

(4) Bertelsen, A.: Meddelelser om Gronland. C. A. Reitzels Boghandel, Copenhagen, 1937. pp. 84-122.

(5) Baarregaard, A.: Dental conditions and nutrition among natives in Greenland. Oral Surg. 2: 995-1007, Aug. 1949.

(6) reported vitamin deficiencies occurring among the Eskimos in the more civilized trading stations in Greenland. Although the modern Eskimo indulges in a relatively softer diet than his forefathers, he partakes of the seal, walrus, and other raw meats, whose fibrous consistency is a factor in the attrition of his teeth as well as the overdevelopment of his muscles of mastication and jaw bone.

CARIES

Pedersen (7) examined 521 primitive Eskimo skulls and found that 0.38 percent showed caries and that 0.08 percent of the permanent teeth examined were carious. Leigh (8) found caries in only 1 percent of 395 primitive Eskimo skulls examined. (My study of skulls at the American Museum of Natural History, New York, and at the Smithsonian Institution, Washington, D. C., verified these facts.) Pedersen examined 1,634 Eskimos on the southwest coast of Greenland and found that in the outposts 39.1 percent had caries in their permanent teeth and that 5.2 percent of the permanent teeth present were carious. At the smaller trading stations the figures were 67.6 and 13 percent, respectively, while at the main trading station they were 87.5 and 29.1 percent.

Baarregaard (5) examined the Eskimos in northwest Greenland and also showed that there has been an increase in the percent of those with caries and a marked increase in the percent of carious teeth as compared with Pedersen's earlier findings.

PERSONAL OBSERVATIONS

In order to study the incidence of caries among the Eskimos I examined, with mouth mirror and explorer, 55 adults (ages 18 to 50 years) and 40 children (ages 6 to 17 years) in the Danish village hospital and in the Eskimo village. A higher percent of interproximal caries might have been discovered if dental roentgenograms had been taken. The size of the sample was limited by the population in the village. The results are shown in table 1. On the basis of these and the afore-mentioned findings of other investigators, the following conclusions may be drawn: (1) the incidence of caries is higher in female adults and children than in males; (2) there has been a progressive increase in the percent of persons with caries and in the percent of carious permanent teeth, as compared with the earlier findings of Pedersen and Baarregaard, in small trading stations; (3) the incidence

(6) Bertelsen, A.: Grøndlansk Medicinsk Statistik Og Nosografi. C. A. Reitzels Boghandel, Copenhagen, 1940. p. 112.

(7) Pedersen, P. O.: Investigations into dental conditions of ancient and modern greenlanders. Dental Record 4: 191-198, 1938.

(8) Leigh, R. W.: Dental pathology of the Eskimo. Dental Cosmos 884-898, 1925.

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of caries among Eskimos is higher in children than in adults; (4) studies of primitive Eskimo skulls show negligible caries rates as compared with the rampant caries observed among the modern Eskimos; (5) Eskimos living in outposts have less caries than those living in main trading stations; and (6) the increase in caries among the Eskimos is in proportion to the increase in their carbohydrate intake.

TABLE 1. *Incidence of caries*

Age (years)	Percent of children with caries in their deciduous and permanent teeth		Percent of deciduous and permanent teeth present showing caries	
	Male	Female	Male	Female
6-17	94.0	95.1	34.2	35.0
	Total: 94.6		Total: 34.6	
	Percent of persons with caries in their permanent teeth		Percent of permanent teeth present showing caries	
	Male	Female	Male	Female
18-50	87.1	92.2	26.1	30.3
	Total: 89.7		Total: 23.2	

Microscopy has shown that there is a higher proportion of microscopic and macroscopic surface irregularity in the enamel of the west Greenland Eskimos than in that of white persons *(9)*. The course of the perikymata is more irregular and the prevalence of lamination and reticulation is much greater in the west Greenland Eskimos than in white persons. An added causative factor in the rampant caries observed in the Eskimo may be a lowered resistance to the penetration of bacteria due to the increased irregularities in their enamel. Although the Eskimos' teeth (ancient and modern) are apparently more susceptible to decay than those of white persons, their increased carbohydrate intake is the most important factor in the increased incidence of caries.

LOCAL (ENVIRONMENTAL) FACTORS AFFECTING OCCLUSION

The percent of malocclusion in primitive Eskimo skulls was reported by Leigh *(8)* as being only 11.4 percent among the

(9) Pedersen, P. O., and Scott, D. B.: Replica studies of surfaces of teeth from Alaskan Eskimo, west Greenland natives, and American whites. Acta odont. Scandinav. 9: 262-292, 1951.

adults. Most of these would fall in Class I. I surveyed the group of Eskimos mentioned above, classifying their occlusion according to the Angle system *(10)*. The results are shown in table 2. Persons whose upper and lower arches were in normal mesiodistal relationship as far as their molars were concerned, but whose upper incisors were in labioversion or in linguoversion to the lower incisors, whose upper anterior teeth were crowded, whose canines were in axioversion, labioversion (fig. 1), linguoversion, or infraversion, who had rotation or buccoversion or linguoversion of the premolar or molar; and in whom the maxillary permanent first molars on both or one side had shifted mesially, although the mandible appeared to be in the proper relationship to the maxilla and cranium were placed in Class I. Open bites and cross bites were included.

TABLE 2. *Distribution of classes of occlusion among Eskimos.*

	Children		Adults	
	Number	Percent	Number	Percent
Normal	17	43.6	32	58.2
Class I (Neutroclusion)	21	53.8	20	36.4
Class II (Div. I and II)	0	0	0	0
Class III	1	2.6	3	5.4
Total	39	100.0	55	100.0

There was no significant difference in the occlusions of the male and female Eskimos. The higher percent of malocclusions in children may be attributed to the fact that part of their teeth were deciduous. Prolonged retention of deciduous teeth or roots and premature loss of deciduous teeth were contributing factors. Carious lesions causing complete or partial loss of the crowns, resulting in drifting of teeth, extrusion, food impactions, and attrition with its concomitant loss of interproximal contacts and incline planes, resulting in periodontal traumatism, were all conducive to local malocclusions among the Eskimos.

Edge-to-edge bites were common among the native adults. Children under 13 showed much less attrition of the occlusal surfaces of the teeth as compared to adults, and showed slight to moderate overbite and overjet of the anterior teeth. Open bites were observed, but posterior cross bites were rare.

The altered diet of the modern Eskimo seems to be a factor in the increase of malocclusions in recent years. The higher

(10) Salzmann, J. A.: Principles of Orthodontics. 2d edition. J. B. Lippincott Co., Philadelphia, Pa., 1950. pp. 476-482.

percent of local anterior deviations (Class I) and normal molar relationships indicate etiologic localized and genetic factors, respectively. Although a large percent of the modern Eskimos possess well-developed jaws and arches in proper mesiodistal relationship, they have a high incidence of caries. There appears to be no correlation between caries resistance, jaw growth and development, and arch relationship in these Eskimos.

Mouth breathing is prevalent among Eskimos *(11)*. The hypothesis, cited by some orthodontists, that mouth breathing causes narrow arches and Class II, Division I malocclusions, is untenable in respect to these mouth-breathing natives with broad-arched palates.

Comparisons of the teeth in primitive Eskimo skulls and modern Eskimos over 35 years of age show a similiar pattern of attrition of the occlusal molar surfaces due to the rugged character of their diet. The occlusal surface slopes down from the higher buccal to the lower lingual cusp on the upper molars, while the lower buccal cusps slope up to the higher lingual cusps on the lower molars. As a result, abnormal forces of mastication are set up during excursions, causing resorption of the lingual alveolar process and gingiva on the upper molars with a concurrent loss of alveolar and gingival structures on the buccal surfaces of the lower molars. The resulting periodontal traumatism not only causes periodontal pockets, but apparently affects the temporomandibular joint, as well.

A study of the temporomandibular articulation of primitive Eskimo skulls reveals resorption of the articular eminence, a reduction of the angle of the articular eminence, and flattened articular surfaces of the condylar head due to resorption. Riesner *(12)* has shown the relationship of edge-to-edge bites to the temporomandibular joint. The coarse consistency of the Eskimo diet may have acted as an orthodontic appliance by obliterating the inclined planes of the occlusal surfaces, thereby transmitting excessive stress during lateral mastication to the temporomandibular joint, resulting in an alteration of these extra-alveolar bony contours and finally causing an edge-to-edge bite.

GENETIC FACTORS

Brash *(13)* revealed the role of genetics in jaw form when he stated: "Such evidence as we have of the inheritance of face and jaw form all points to the genetic condition as a pri-

(11) Footnote reference *(10)*. p. 423.

(12) Riesner, S. E.: Temporomandibular reactions to occlusal anomalies. J. Am. Dent. A. 25: 1938-1953, Dec. 1938.

(13) Brash, J. C.: The Aetiology of Irregularity and Malocclusion of the Teeth. Dental Board of the United Kingdom, London, 1929. pp. 191-246.

mary factor." Krogman *(14)* analyzed "race-mixture data and found that face height and byzygomatic breadth were phenotypically dominant although modifiable, and that in a Mongoloid-Caucasoid cross bizygomatic breadth was dominant over height. Greater mandibular (gonial) breadth is dominant as is also progenia." The predominance of normal and Class I occlusions in the modern Eskimo dentition compares favorably with the primitive, indicating a hereditary dominance.

The controversial problem of whether the broad U-shaped arches of the Eskimo are the result of increased function or due to hereditary influences is frequently encountered during the study of the dentofacial complexes of these people.

Waugh *(15)* stated, "...we have come to believe that the size of the body of the jaw is determined largely by heredity and form; quantity and size of the alveolus are primarily the result of function." The transverse diameter of the palate is attained for the most part by growth in the median palatine suture. Watt and Williams *(16)* stated that "the mastication of foods that require vigorous function is likely an important stimulus in the growth in width of the maxilla in young animals, but in adult animals (rats), after the growth sutures have fused, further increase in width is impossible." The transverse palatal diameters of the adult Eskimos I examined showed variable thickened alveolar processes, particularly in the molar area, as compared with those of the children. I concluded that because an adult had used his teeth for a longer time, his alveoli had adapted to the functional stress by the apposition of supporting bone.

Because the width of the transverse palatal arch would be a variable measurement depending on the physical consistency, musculature, et cetera, I decided to delineate the genetic factor by measuring the palatal arch widths with a Boley gage as follows:

Intermolar width. The width of the palate was measured posteriorly between points on the buccal surfaces of the first molars. These points were taken between the middle and distobuccal cusps.

The *intercanine width* was taken between the maxillary canines at the height of greatest curvature on the labial surfaces at about the midpoint of the mesiodistal diameter.

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(14) Krogman, W. M.: Inheritance of non-pathologic physical traits in man. Eugenical News 21: 139-146, Nov.-Dec. 1936.

(15) Waugh, L. M.: Influence of diet on jaws and face of American Eskimo. J. Am. Dent. A. 24: 1640-1647, Oct. 1937.

(16) Watt, D. G., and Williams, C. H. M.: Effects of physical consistency of food on growth and development of mandible and maxilla of rat. Am. J. Orthodontics 37: 895-928, Dec. 1951.

TABLE 3. *Maxillary arch widths*

	Number	Intermolar			Intercanine		
		Mean (mm.)	Range (mm.)	Standard deviation (mm.)	Mean (mm.)	Range (mm.)	Standard deviation (mm.)
Modern Eskimo boys (Age 8-12 years)	14	56.4	52-60	±1.53	38.9	34-41	±1.67
Modern Eskimo girls (Age 8-12 years)	16	55.7	52-62	±2.66	38.6	34-41	±2.15
Modern male adult Eskimo	27	60.6	57-64	±1.84	41.1	35-47	±2.17
Modern female adult Eskimo	27	58.2	54-64	±2.14	39.9	35-42	±2.004
Primitive male adult Eskimo skulls	13	61.4	56-64	±2.53	40.0	36-43	±2.15
Primitive female adult Eskimo skulls	13	57.6	54-62	±2.30	38.7	32-42	±2.79

Analysis. The maxillary intermolar and intercanine arch widths are shown in table 3. The palatal arch widths of the male (primitive and modern) are larger than those of the female. Furthermore, the similarity of measurements (mean, range, and standard deviation) indicate an inherent genetic pattern between primitive and modern Eskimos insofar as palatal arch width is concerned.

Measurements of the palatal arch widths of Eskimo children between the ages of 8 and 12 years showed that 93.1 percent of the mean adult male intermolar arch width was attained in boys and 95.7 percent was attained in girls; 96.8 percent of the mean adult intercanine arch width was attained in boys and 96.7 percent was attained in girls.

The fact that the modern Eskimo's diet has been altered in comparison with the primitive Eskimo does not seem to have affected the intercanine and intermolar arch widths, but the transverse palatal dimension between the 2 bucco-alveolar processes may be affected in proportion to the masticatory forces. This is merely another corroboration of the plasticity of bone in responding to functional stress. Furthermore, on the basis of the similarity of palatal arch widths and the prevalence of normal occlusions, it can be stated that despite the intermixture of white racial strains, the normal, molar mesiodistal relationships, and the broad, well-developed arches of the natives are genetically dominant.

CONCLUSIONS

The diet of the primitive Eskimo contained all the vitamins and minerals essential for normal dental health. That of the modern Eskimo includes a greater proportion of carbohydrate foods. Primitive Eskimos had practically no caries, but dental decay is becoming increasingly prevalent among the modern Eskimos. A greater percent of malocclusion was observed among modern as compared with primitive Eskimos. Most of the adults observed had normal occlusions. Most malocclusions were Class I; none were Class II; and a small percent were Class III. The tendency toward inheritance of normal occlusion among the Eskimos appears to be greater than that toward inheritance of abnormal occlusion although variations were observed. Edge-to-edge bites were prevalent among adults, while children under 14 years of age showed overbites and overjets. Edge-to-edge bites could be considered the result of the abrasive quality of the diet.

The altered diet of modern Eskimos seems to be a factor in the increase of malocclusions as compared with primitive Eskimos. The greater percent of local anterior deviations (Class I)

and normal molar mesiodistal relationships indicate localized etiologic and genetic factors respectively. There appears to be no correlation between caries resistance and jaw growth and development, or between caries resistance and arch relationships in the Eskimos.

The opinion that mouth breathing is an etiologic factor in narrow arches and Class II malocclusions is untenable among the mouth-breathing Eskimos with broad-arched palates. The physical consistency of the Eskimo diet has caused attrition of the occlusal surfaces of the teeth, periodontal traumatism, and seems to have caused an alteration in the bony contours of their temporomandibular joints.

As far as the molar mesiodistal relationship (occlusion) and palatal arch widths and contours are concerned, there has not been sufficient intermixture of white racial strains nor change in the type of diet to suppress the previously mentioned dominant hereditary factors in the Eskimos which have been stabilized through centuries of natural selection and inbreeding.

BOOK REVIEW

Clinical Progress in Cardiovascular Disease, edited by *Herman L. Blumgart*, M. D., Physician-in-Chief, Beth Israel Hospital, and Professor of Medicine, Harvard Medical School, Boston, Mass. Modern Medical Monographs, No. 2. 143 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., publishers, 1952. Price $4.50.

Since December 1950 Circulation has published authoritative critical reviews on recent advances in cardiovascular disease. This small book contains all the reviews published from December 1950 through July 1952. A wide variety of subjects has been selected. The editors of Circulation are to be commended for their choice of subjects and authors. Most of the essays are devoted to the clinical aspects of cardiovascular disease. They are authoritative, brief but to the point, and complete. An adequate bibliography is included with each essay. This small volume is heartily recommended, particularly to those who do not have ready access to the original articles.

—*Col. E. M. Goyette, MC, U. S. A.*

ANALYSIS OF CESAREAN SECTIONS[1]

L. MARSHALL HARRIS, *Captain, MC, U. S. N.*

JAMES M. JONES, *Lieutenant, MC, U. S. N.*

THE following observations relating to indications for, incidence of, and statistics on cesarean sections were made after reviewing the records of the obstetric and gynecology services at this hospital for the period of 1 July 1950 to 1 July 1951. The source of clinical material is varied in that many of our patients were referred or transferred from different parts of the country and from abroad; and it is controlled in that only dependents of active duty Navy and Marine Corps personnel were eligible for treatment. Antenatal care is somewhat standardized and is given in the clinic either at the Naval Dispensary in Washington, D. C., or at this hospital, both under the cognizance of the chief of the obstetrical service at the hospital. All antenatal patients are sent to the hospital for delivery and postpartum treatment and all patients who present obstetrical difficulty are referred to the hospital for consultation and for admission as indicated.

There were 1,961 deliveries on the service in the stated period with 46 cesarean sections, or an incidence for the period of 2.3 percent. The current annual number of deliveries would be much higher with a monthly average of about 225 deliveries. The current cesarean section rate is 4.8 percent, figured on the basis of the 3 months ending 29 February 1952. The average rate for 10 of the larger civilian hospitals is about 4.9 percent. All patients are delivered by an obstetrical resident and with consultation, evaluation, and disposition as to type of treatment and/or delivery by the chief of service.

The trend toward liberalization in the indication for abdominal delivery (reflected in the above figures) has been influenced by more adequate evaluation, better-trained obstetricians, and the advent during the past few years of the blood bank, antibiotics, chemotherapy, and improved hospital facilities. We are basically in accord with this liberalization but each patient must be considered individually. Our present policy does not necessarily mean adherence to the dictum "once a cesarean section, always a cesarean," but consideration of the source of our patients, the existing low morbidity and mortality rates, and improved facilities seems to justify such practice in most cases.

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Table 1 shows the age incidence of the patients who were delivered by cesarean section. Table 2 shows their parity. This indication was disregarded in 25 patients who had had previous section. A low cervical operation was performed on 40 patients. The classical operation was performed on 6 patients in whom sterilization was to be accomplished or in whom marked varicosities, adhesions, or tumors in the lower uterine segment made this the operation of choice. The low lying placenta has not been accepted in this hospital as an absolute indication for the classical operation. In 6 patients with placenta praevia who had moderate to marked blood loss the pregnancy was terminated by cesarean section in only 2. In all patients with placenta praevia it is routine to prepare for cesarean section by arranging for blood for transfusion and examining the patient in the operating room under "double setup" in which a sterile vaginal examination is performed and, if section is found to be indicated, the abdomen can be prepared without removing the patient from the table. Whether the transverse or the longitudinal incision was used was largely left to the physician's preference, but such factors as varicosities and rotation of the uterus influenced his choice in some cases.

TABLE 1. *Age of 46 patients delivered by cesarean section*

Age (years)	Number
18-19	1
20-29	25
30-39	17
40 or over	3

TABLE 2. *Parity of 46 patients delivered by cesarean section*

Para	Number
0	12
1	19
2	12
4 or more	1

The indications are shown in table 3. In some patients there was more than one indication. Cephalopelvic disproportion was determined by trial of labor and roentgenographic pelvimetry. Uterine inertia is often seized on by the impatient and uninitiated as an indication for cesarean section in that relatively rare patient, who, for one reason or another, fails to meet our expectations in so far as the progress of labor is concerned. In 2 of our 3 patients with uterine inertia, the ineffective uterine contractions persisted in spite of the use of analgesics, rest, parenteral fluids, and oxytocics. After 30 or more hours of desultory labor with no progress the patients became exhausted and an elective low cervical section with antibiotics and transfusion of whole blood was accomplished. These patients were primigravidas. There was no evidence of the so-called Bandl's ring and with alpha-hypophamine given by intravenous drip there was no postpartum hemorrhage. In 1 of these patients irregularity of the fetal heart influenced the decision to intervene, but in both cases viable infants were deliver-

ed. The third patient had ineffective uterine contractions in the presence of uterine fibroids and elective section was accomplished after 36 hours with poor progress, moderate uterine bleeding, and evidence of fetal distress.

TABLE 3. *Indications for cesarean section*

Indication	Number
Previous section	25
Cephalopelvic disproportion	10
Abruptio placentae	5
Uterine inertia	3
Toxemia	3
Placenta praevia	2
Previous vaginal plastic surgery	2
Diabetes	2
Elderly primigravida	1

The diagnosis of abruptio placentae was made early from the history of sudden pain and tetanic contractions (with external bleeding in 3 of the 5 patients and without external bleeding in 2). The signs and symptoms presented on admission were diagnostic and in 3 patients the cervix on examination under double setup was found to be long, firm, and undilated and the fetal heart sounds were inaudible. Pain increased with increase of tetanic contractions and enlargement of the uterus. The condition of the mother became poor and an elective section was performed. In 2 deliveries a nonviable fetus was obtained and in 3 the fetus required prolonged resuscitation but survived. In 2 patients the shuttle gauze method (gauze was forced down into the vagina from above) was resorted to in addition to continuous alpha-hypophamine given by intravenous drip and in 3 oxytocics alone were used. None of the patients had postpartum hemorrhage.

The patient who was classified as an elderly primigravida was 43 years of age and very anxious for a baby. She had a borderline contraction of the pelvis and an elective cesarean section was performed. The patients with toxemia of pregnancy were sectioned in the interest of both mother and fetus after conservative efforts failed to bring the toxemia under control in the presence of an undilated, unripe cervix from 1 to 6 weeks from term. The patients were definitely pre-eclamptic, failed to respond to treatment after adequate therapy, and presented a problem as to fetal survival. Two of the infants died following delivery. One death was attributed to abruptio placentae and prematurity associated with toxemia.

The diabetic patients were controlled medically up to the thirty-seventh and thirty-eighth weeks, respectively. Because of roentgenographic evidence of excessively large fetuses, a history of the loss of 2 and 3 babies, respectively, and the relative fetopelvic disproportion abdominal delivery was accomplished. Both infants survived.

In this series spinal anesthesia was used on 39 patients, procaine locally supplemented by pentothal in 3, cyclopropane in 3, and ether in 1.

A member of the anesthesia staff is on call at all times so that the obstetrician may have the agent of choice with the guidance, experience, and co-operation of the anesthetist. There were complications in 4 patients. One developed thrombophlebitis, one a superficial infection in the incision, one an unexplained rise in temperature above 100.4° F. on 2 occasions, and one 48 hours prior to cesarean section had rupture of the membranes with a discharge of purulent amniotic fluid. None of the mothers in this series died but there were 5 fetal deaths. One was delivered 16 days after the expected date of confinement. The mother had had a previous cesarean section. She was delivered under cyclopropane anesthesia of an infant weighing 4 lb. 11 oz. who died 2 days later. Autopsy revealed cerebral hemorrhage, pulmonary atelectasis, and prematurity. The second was delivered 14 days after the expected date of confinement. The mother had uterine inertia and spinal anesthesia was used. The baby weighed 7 lb. 2 oz. at birth and died in the first day of congenital pulmonary atelectasis. The third was delivered under cyclopropane anesthesia to a mother who had had a previous cesarean section. The infant was anencephalic. The fourth was delivered under spinal anesthesia to a mother who had eclampsia and abruptio placentae. The infant weighed 2 lb. 14 oz. and autopsy revealed prematurity and intraventricular hemorrhage. The fifth was delivered under ether anesthesia to a mother who had abruptio placentae. The infant weighed 6 lb. and was stillborn.

PRIMARY HYPERLIPEMIA

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PRIMARY hyperlipemia is a relatively rare disease. Only 19 cases have been reported in the literature. The first case of primary hyperlipemia was reported by Bürger and Grütz (2). Movitt et al. (3) tabulated a total of 14 cases and added 3 cases of their own. Case reports of only 2 other patients with this disorder have been published to our knowledge. One was reported by Koszalka and Levin (4) and the other by Dunphy (5). In this condition an excessive amount of fat or lipids are found in the serum and it is recognized by the milky, opaque appearance of the serum (4). Movitt et al. (3) stated that primary hyperlipemia is a disorder of fat metabolism characterized by hyperlipemia of the retention type, frequently accompanied by hepatosplenomegaly, eruptive xanthomatosis, and abdominal pain or discomfort. Thannhauser (6) reported that the milky appearance of the serum is usually due to an increase in the neutral fat content above 150 percent of the normal value. He also found that an increase of cholesterol or phospholipids without an increase of the neutral fat never causes a milky serum (7). Ahrens and Kunkel (8) pointed out that if the amount of phospholipid in plasma is 30 percent or more of the total lipids, the plasma will be clear and appear nonlipemic even at total lipid levels as high as 3,000 mg. per 100 cc.; but if it is less than 30 percent, the plasma will be cloudy and appear

(1) Reese Air Force Base, Tex., at time of writing.

(2) Bürger, M., and Grütz, O.: Über hepatosplenomegale Lipoidose xanthomatösen Veränderungen im Haut und Schleimhaut. Arch. f. Dermat. u. Syph. 166: 542-575, Oct. 1932.

(3) Movitt, E. R.; Gerstl, B.; Sherwood, F.; and Epstein, C. C.: Essential hyperlipemia. Arch. Int. Med. 87: 79-96, Jan. 1951.

(4) Koszalka, M. F., and Levin, J. J.: Idiopathic hyperlipemia. Ann. Int. Med. 33: 473-480, Aug. 1950.

(5) Dunphy, E. B.: Ocular conditions associated with idiopathic hyperlipemia. Am. J. Ophth. 33: 1579-1586, Oct. 1950.

(6) Thannhauser, S. J.: Lipidoses: diseases of cellular lipid metabolism. In Christian, H. A.: Oxford Medicine. Oxford University Press, New York, N. Y., 1949. Vol. 4, Pt. 2, p. 595.

(7) Thannhauser, S. J.: Medical progress; serum lipids and their value in diagnosis. New England J. Med. 237: 515-522, Oct. 2, 1947.

(8) Ahrens, E. H., and Kunkel, H. G.: Stabilization of serum lipid emulsions by serum phospholipids. J. Exper. Med. 90: 409-424, Nov. 1949.

lipemic even at fairly low levels. Sorenson *(9)* remarked that "the perfect clearness of such liquids as serum and plasma, in spite of their contents of lipoids, is explicable only by assuming linkage between lecithin and sterols on the one hand and the protein on the other." Synonyms for this disorder are idiopathic familial lipemia and essential hyperlipemia *(6)*.

CLASSIFICATION

Koszalka and Levin *(4)* classified hyperlipemia as primary (idiopathic) and secondary. Secondary hyperlipemia may be associated with (1) the ingestion of an excess of fat, (2) von Gierke's disease, (3) starvation, (4) blood dyscrasias, (5) lipoid nephrosis, (6) nephrotic state of chronic glomerulonephritis, (7) hypoproteinemia, (8) obesity due to overnutrition, (9) pregnancy, (10) hypothyroidism, (11) diabetes mellitus, (12) pancreatic disease, (13) liver disease, and (14) the lipoidosis (found in essential xanthomatosis or in Niemann-Pick's disease and in which milky serum is not found as a rule).

To the above list, Movitt et al. *(3)* add as causes of the secondary type, thrombosis of the renal veins, poisoning, and anoxemic and cachectic states. Atlas et al. *(10)* recently reported a case of hyperlipemia associated with primary amyloidosis. Rich et al. *(11)* produced hyperlipemia in rabbits by the administration of cortisone.

ETIOLOGY

The etiology is unknown. The mechanism apparently is similar to a prolonged postprandial hyperlipemia. Fat is absorbed in the usual way but does not go out through the capillaries to the places of metabolism with normal rapidity. The term "retention hyperlipemia" has therefore been coined to describe this condition *(12)*. Thannhauser *(7)* stated that primary idiopathic hyperlipemia may occur as an inherited disorder or it may occasionally be observed with and without secondary eruptions of skin xanthomatoses.

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(9) Sorenson, S. P. L.: Constitution of soluble proteins (reversibly dissociable component systems). Compt. rend. d. trav. du lab. Carlsberg 18: 1-124, Apr. 1930. Quoted in Gould, R. G.: Lipid metabolism and atherosclerosis. Am. J. Med. 11: 209-227, Aug. 1951.

(10) Atlas, D. H.; Gaberman, P.; and Stern, K.: Primary amyloidosis associated with hyperlipemia and hypercholesterolemia; report of case. Am. J. Clin. Path. 20: 371-376, Apr. 1950.

(11) Rich, A. R.; Cochran, T. H.; and McGoon, D. C.: Marked lipemia resulting from administration of cortisone. Bull. Johns Hopkins Hosp. 88: 101-109, Jan. 1951.

(12) Block, W. J., Jr.; Mann, F. D.; and Barker, N. W.: Effect of small doses of heparin in increasing translucence of plasma during alimentary lipemia; studies in normal individuals and patients with atherosclerosis. Proc. Staff Meet., Mayo Clin. 26: 246-249, June 20, 1951.

CASE REPORT

A 20-year-old man was admitted on 8 February 1951 with a severe local reaction to a smallpox vaccination on his left arm. On the next day the laboratory reported that a serologic test could not be performed on this patient's serum because it was opaque and milky in character. The patient entered military service on 6 January 1951 and was vaccinated on 11 January. He had not been vaccinated previously. On 13 January blood was drawn from his arm for a serologic test. He was not notified of any abnormality at this time. Eleven days after vaccination he reported on sick call complaining of swelling, redness, and tenderness about the site of vaccination. He received several injections of penicillin at this time.

On admission, there was an ulcer, 2 cm. in diameter and 1 cm. deep, filled with black necrotic tissue, on the lateral aspect of the left arm. It was surrounded by a large area of induration and redness. There were several tender, walnut-sized lymph nodes in his left axilla. His temperature was normal. Repeated examinations of the eyegrounds failed to reveal evidence of lipemia retinalis, but the vascular light reflexes of the retinal arterioles had greater breadth than is usually seen in a person 20 years of age. The other 2 ocular manifestations of hyperlipemia *(5)* (lipid interstitial keratitis and xanthomas of the eyelids) were not present. The patient's stay in the hospital was uneventful. Antibiotics and soaks controlled his infection and the ulcer of the arm was eventually replaced by firm scar tissue.

The results of the lipid tests are shown in table 1. The amount of total lipids on admission was more than 6 times the upper limit of normal. Neutral fat was not determined as such. Two types of therapy were tried. A low-fat diet of 2 weeks' duration resulted in a normal-appearing blood serum. The total lipid content at this time (800 mg. per 100 cc.) was not far above the upper limit of normal. Desiccated thyroid, up to 0.2 gram per day, was then given empirically while the patient was on a normal diet. The serum was milky in appearance before and after this trial. BMR's before thyroid therapy were +13, +16, and +24. After 10 days of thyroid therapy the rate was +30.

Block et al. *(12)* recently found that small doses of heparin given intravenously to normal persons with alimentary hyperlipemia caused an increase in the translucency of the serum within 15 minutes. Accordingly, 20 mg. of heparin was given intravenously to this patient but no decrease in the milkiness of the serum was noted in 15 minutes. On 2 August the cholesterol protein conjugate (12-20 Svedberg flotation units) was 0 mg. per 100 cc. (fig. 1). The electrophoretic serum partition showed:

TABLE 1. *Blood lipid studies (in mg. per 100 cc.)*

	Normal	On admission (9 Feb.)	Before low-fat diet (19 Apr.)	After low-fat diet (26 Apr.)	After thyroid therapy (2 May)	On ordinary diet (3 Oct.)
Total lipids	450-650	4,020.0	1,320.0	800.0	1,110.0	3,300
Fatty acids	310-460	3,597.6	1,093.0	617.2	927.0	2,997
Lipid phosphorus	10-14	21.9	—	7.7	2.2	9.76
Total cholesterol	150-250	248.8	226.2	182.8	183.0	303
Cholesterol esters	80-180	38.2	100	71.8	61.9	65.1
Lecithin	78	—	452.5	—	—	—

albumin, 53 percent; alpha 1 globulin, 3 percent; alpha 2 globulin, 10 percent; beta globulin, 13 percent; gamma globulin, 21 percent; A/G ratio, 1.1; and total proteins, 7.56 grams per 100 cc.

Because of the unpublished observations of Harvill, adenosine-5-monophosphate was administered to determine whether it would lower the blood cholesterol level. Beginning on 2 August, 1 cc. of this drug was injected intramuscularly every 2 days for 3 doses. On 7 September this was repeated.

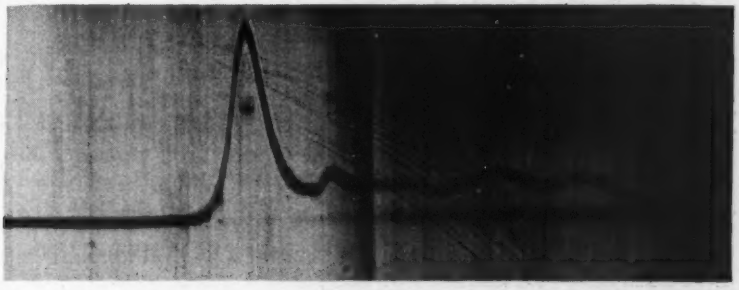

Figure 1.

Before administration of adenosine-5-monophosphate in August there were 2,624 mg. of cholesterol per 100 cc. of mixed blood serum (209 in the clear portion of the serum) and after administration of the drug there were 740 mg of cholesterol per 100 cc. of mixed blood serum (175 in the clear portion). In September there were 478 mg. of cholesterol per 100 cc. of serum before administration of the drug and 374 after.

On admission the erythrocyte count was 5,430,000 with 15.85 grams of hemoglobin. The leukocyte count was 8,500 with 68 percent neutrophils, 26 percent lymphocytes, and 6 percent monocytes. Subsequent blood counts showed no essential change. The platelet count was 300,000. The bleeding time was 1 minute. The blood coagulation time was 6½ minutes.

The nonprotein nitrogen was 47; serum lipase, 0.3 cc.; alkaline phosphatase, 3.34 Bodansky units; acid phosphatase, 2.32 Bodansky units; serum phosphorus, 5.6 mg. per 100 cc.; and serum amylase, 8 units. The total protein on admission was 9.6 grams per 100 cc. The A/G ratio was reversed at this time; albumin, 3.5 grams per 100 cc. and globulin, 6.1 grams per 100 cc. Serial blood protein studies during convalescence from the infected vaccination showed reversion to normal values 3 weeks after admission. Five minutes after injection of bromsulphalein, 82 percent was still present in the blood and at the end of 30 minutes, 4.5 percent was present. The prothrombin

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time was 100 percent. Four hours after the oral administration of 6 grams of sodium benzoate, a total of 3.9 grams of hippuric acid was recovered from the urine.

COMMENT

This patient has been followed for 6 months since his hyperlipemia was discovered. There has been no change in the milky appearance of blood serum in that time. The only factor which decreases the amount of fat in his blood is a low-fat diet. This is in accordance with the experience of other authors. The cholesterol level in mixed serum is much higher than that in clear serum. The significance of the low percentage of esters as compared to total cholesterol is unknown. In this patient, the total cholesterol level was not much above normal when the clear portion of the blood serum was analyzed. When the mixed milky serum was analyzed, there was a marked increase in the cholesterol level. The only known treatment of this condition is a low-fat diet. The prognosis is considered to be good and premature arteriosclerosis probably does not develop in these patients *(12)*. When last seen this patient was performing his military duties in a satisfactory manner.

BOOK REVIEW

Practical Pharmacology, by *J. H. Burn*, Professor of Pharmacology, University of Oxford, Illustrations by *E. M. Vaughan Williams*. 72 pages; illustrated. Blackwell Scientific Publications, Oxford, England, publisher, 1952. Published simultaneously in the United States by Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $3.25.

This book presents 21 groups of experiments, designed to be performed before a class, and represents the work of several people who have had a share in developing the present course in practical pharmacology offered at the University of Oxford. The work is presented in a clear, easily assimilated form and the illustrations are well prepared and helpful. It is interesting and useful as a reference book and is fairly comprehensive, but its value as a text in the United States would be doubtful, because some of the methods described are not used in this country.

—*Commander R. L. Taylor, MSC, U. S. N.*

SYPHILITIC ANEURYSM OF THIRD PORTION OF THE SUBCLAVIAN ARTERY

EUGENE D. ERMAN, *Major, MC, U. S. A. (1)*

REPORTS of the successful removal of a syphilitic aneurysm of the third part of the subclavian artery and the first and second parts of the axillary artery are rare. The threat of rupture and fatal hemorrhage is a specific indication for resection of such lesions when accessible. Daniel *(2)* recently reported the successful removal of 2 syphilitic aneurysms, both of the first portion of the subclavian artery. He stressed the facility with which these tumors were removed by opening the pleural cavity. Temple *(3)* also entered a plea for the transpleural exposure in approaching the first part of the subclavian artery. He described the collateral circulation after ligation of the first part of the subclavian artery on the left side.

CASE REPORT

A 52-year-old Negro was admitted to this hospital on 30 July 1951 complaining of swelling in the left supraclavicular area of 2 weeks' duration. When first noted, the swelling was the size of a small plum. It was associated with minimal pain. The patient had no knowledge that he had syphilis.

His eyegrounds showed slight tortuosity of the vessels and arteriovenus nicking in a ratio of 1:2. The left side of his neck contained a fullness which on admission measured 2 cm. in elevation by 2 by 4 cm. (fig. 1). The mass was bounded anteriorly by the clavicle, medially by sternocleidomastoid muscle, and laterally it disappeared gradually under the deltoid muscle. The veins of his neck on the left side were markedly distended and the mass pulsated synchronously with the heart beat and the radial pulse. There was no edema of either arm or hand. The blood pressure in his right antecubital fossa was 215/140 and in his left, 180/140. The peripheral arteries pulsated normally except for his left radial artery and this pulsated much more weakly than his right but was palpable. Moderate perspira-

(1) Gorgas Hospital, Ancon, C. Z.

(2) Daniel, R. A., Jr.: Syphilitic aneurysm of subclavian artery. Ann. Surg. 134: 251-258, Aug. 1951.

(3) Temple, L. J.: Aneurysm of first part of left subclavian artery; review of literature and case history. J. Thoracic Surg. 19: 412-421, Mar. 1950.

tion was noted equally on both hands and arms. There was mild clubbing of the fingernails of his left hand. A blowing bruit was heard over the mass on auscultation. His heart was enlarged 2 cm. outside of the left midclavicular line and 3 cm. to the right of the sternal margin. His sounds were of good quality and there was a grade 2 systolic murmur at the apex.

Figure 1. Photograph of patient before operation showing swelling in the left side of the neck.

His erythrocyte count was 3,460,000. His hemoglobin was 11.2. His leukocyte count was 5,900. His Wassermann reaction was 4 plus. His spinal fluid cell count was 30. The total protein in the spinal fluid was 161 mg. per 100 cc. The colloidal gold curve was 5555442100. A roentgenogram of the chest revealed cardiac enlargement and marked tortuosity of the thoracic aorta. Arteriograms following injection of iodopyracet into the pulsating mass in the left retroclavicular area revealed a large aneurysmal dilatation of the lateral portion of the subclavian artery measuring 4 cm. in diameter (fig. 2). There was no evidence of communication with the venous system.

With the patient under general anesthesia, a curvilinear incision was made over the medial half of the clavicle. The periosteum of the clavicle was incised and the medial 2/3 of the clavicle were removed subperiosteally. The periosteum and subclavius muscles were incised. The clavicular origin

of the pectoralis major and minor was cut. This maneuver afforded excellent exposure of the mass. Blunt dissection was used to expose the subclavian, axillary, and cephalic veins. The subclavian and axillary veins were fused posteriorly to the aneurysm and were removed with the aneurysm. The cephalic

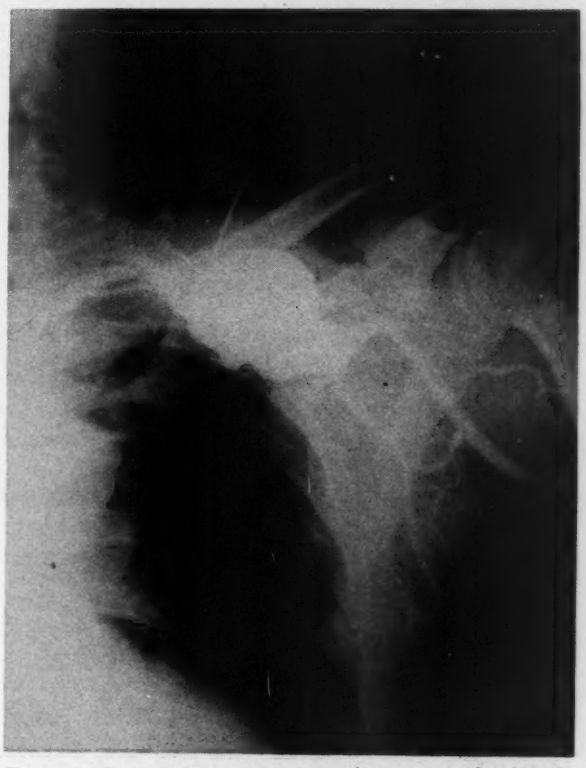

Figure 2. Preoperative arteriogram of aneurysm showing the border of the lesion in the lateral third of the subclavian artery. (This finding facilitated accurate extrapleural surgical approach.)

vein was tied proximally and distally with No. 00 black silk and cut. The proximal side of the subclavian vein was doubly tied with No. 1 silk and then transfixed with No. 00 silk and cut. The distal portion of the exposed vein (second portion of the axillary vein) was tied similarly and cut. The scalenus anterior muscle was cut from its attachment to the first rib and the subclavian artery coursing up from the mediastinum over the first rib was then easily identified and dissected free.

An umbilical tape was slipped around the artery and left in place while further dissection of the aneurysm was performed. The umbilical tape was then tied, thereby stopping the arterial supply and pulsation of the aneurysm. Two No. 00 black silk ligatures, one a transfixion suture, were placed distally and the artery was cut. The axillary artery was tied doubly with No. 00 silk, transfixed in its third portion, and cut. The aneurysm was freed from its adjacent structures, including the anterior, lateral, and posterior cords of the brachial plexus and the subscapularis muscle. The subscapular artery was found to leave the posterolateral surface of the aneurysm and it was doubly ligated with No. 00 silk and cut. No other arteries leading from the aneurysm were found. The wound was closed in layers. Drainage of the subcutaneous space was accomplished with a split Penrose rubber drain.

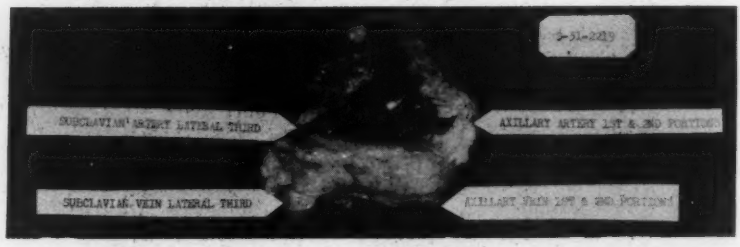

Figure 3. Anterior surface of aneurysm with sac opened.

Gross examination after operation revealed an aneurysmal dilatation of the last part of the subclavian artery and the first and second parts of the axillary artery which measured 4½ by 4½ by 5 cm. The bulk of the aneurysm protruded superiorly. The wall of the aneurysm was 3 mm. thick and was partially filled by a laminated clot which was 1 cm. thick. Several small patches of stellate wrinkling were seen on the intimal surface of the artery in the aneurysm. A 6-cm. length of the accompanying vein was attached to the anterior surface of the artery (fig. 3).

Microscopic sections revealed extensive obliterative endarteritis of the vasa vasorum with dense, perivascular collections of plasma cells and lymphocytes. The intima was moderately thickened. In some areas, however, the endothelial lining was absent, the intima was thin, and the laminated clot was adherent to the free surface. The elastic fibers of the media were fragmented. A pathologic diagnosis of syphilitic aneurysm was made.

The patient was afebrile after the third day. There was no postoperative swelling of his left arm. His left radial pulse

was not palpable after the operation but his left hand and arm were only slightly less warm than his right. His blood pressure could not be obtained in the left arm after the operation and in the right arm was unchanged. On the seventh postoperative day his skin sutures were removed and the wound was well healed. Physiotherapy was started and the range of motion of

Figure 4. Postoperative venogram showing collateral venous return after ligation of cephalic and axillary veins.

his left arm gradually increased. Within 12 days after operation he had regained complete function. Thirteen days postoperatively a subcutaneous pocket of 50 cc. of sterile serum was aspirated from the lateral border of the incision. Several aspirations were performed during the next few days for the removal of small amounts of serum. Eighteen days after operation no further aspirations were necessary.

One month after operation a venogram of the left shoulder girdle revealed the channels through which the venous blood returned from the arm to the shoulder girdle and chest wall (fig. 4). It is believed that the collateral arterial supply to the arm accompanies the demonstrated venous return. Two months after operation there was no edema of the left hand or arm. Slight venous distention was noted over the arm and shoulder. The left radial artery was not palpable and the blood pressure

was not obtainable. In spite of the absent pulse and blood pressure, function of the left upper extremity was normal and the skin was only slightly less warm than that of the right. Six months after surgery no change was noted in the patient's condition.

DISCUSSION

Unilateral clubbing of the fingers has been reported previously (2, 4). Although the clubbing was not marked in this patient, it was definitely present. Of special interest in this patient is the unusual preoperative arteriogram which accurately delimited the medial border of the lesion and made preoperative planning of the approach a relatively simple matter. Because the arteriogram showed no involvement of the first part of the subclavian artery, the approach to this tumor was extrapleural. Resection of the clavicle gave adequate exposure. The aneurysm of the subclavian artery was situated lateral to the origin of both the thyrocervical axis and the internal mammary arteries and it lay medial to the anterior and posterior circumflex branches of the axillary artery. Collateral circulation was adequate from the moment of ligation. Undoubtedly, the laminated intramural clot had caused collateral arterial channels to become well established during the progression of growth of the aneurysm.

(4) Brooks, B.: Aneurysm of axillary artery; case of spontaneous aneurysm of first portion of axillary artery associated with unilateral clubbing of fingers and Dupuytren's contracture. S. Clin. North America 10: 741-755, Aug. 1930.

BOOK REVIEW

The 1951 Year Book of Endocrinology (January 1951-January 1952), Edited by *Gilbert S. Gordan*, M. D., Ph. D., Assistant Professor of Medicine, University of California School of Medicine, Assistant Physician, University of California Hospital; Consultant Endocrinologist, Langley Porter Clinic of the State Department of Mental Hygiene, San Francisco, Calif. 415 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1952. Price $5.

This book admirably covers the rapid advances made in clinical endocrinology. The current literature has been expertly summarized, and is all the more valuable because of the many pertinent, authoritative editorial comments. Such a year book is especially useful to the busy physician who does not have ready access to the original publications. —*Col. R. E. Blount, MC, U. S. A.*

METHOD OF DETERMINING INTRAMEDULLARY NAIL SIZE AND LENGTH

AUGUST W. SPITTLER, *Colonel, MC, U. S. A.* (1)

JOHN J. BRENNAN, *Lieutenant Colonel, MC, U. S. A.* (1)

FIXATION of a femoral fracture with an intramedullary nail necessitates a simple method of determining accurately before operation the exact length and medullary canal dimensions of the femur. A simple device to facilitate accurate measurement of femoral length and canal width is herein presented. This has been successfully employed at this hospital for 2 years.

The first method to be used for determining exact bone measurements was that introduced by Millwee (2). This was called "slit scanography." In this method a roentgenographic table with a side nail and arm is used. The arm holds the roentgen tube at a set target distance and the tube is propelled lengthwise in relation to the table at set speeds by a motor-driven gear. An adjustable slit cone is used between the tube and the patient. This reduces the effect of distortion and variation of density. Direct measurement on the developed film determines bone length.

Mueller and Higgason (3) reported the "spot scanography" method of determining bone length. The patient is placed on a roentgenographic table in a supine position with a 14- by 17-inch film under the thigh. A roentgen tube, with a small circular cone, is centered directly over the proximal end for one exposure and over the distal end of the femur for a second exposure. The patient is not moved between exposures. From the roentgenogram, a direct measurement of the femoral length is possible.

Bell and Thompson (4) reported a "modified spot scanography" method in which a steel rule 1/64-inch thick is placed on the

(1) Walter Reed Army Hospital, Washington, D. C.

(2) Millwee, R. H.: Slit scanography. Radiology 28: 483-486, Apr. 1937.

(3) Mueller, W. K., and Higgason, J. M.: Spot scanography; method of determining bone measurement. Am. J. Roentgenol. 61: 402-403, 1949.

(4) Bell, J. S., and Thompson, W. A. L.: Modified spot scanography. Am. J. Roentgenol. 63: 915-916, June 1950.

center line of the roentgen table. The part to be exposed is centered to the steel rule and the cassette is covered with a sheet of lead having 2 holes, each 4 inches in diameter, which can be closed. These are centered also for upper and lower ends of the femur. From 2 exposures any 2 points at opposite bone ends can be readily calculated from the reading of the ruler on the film.

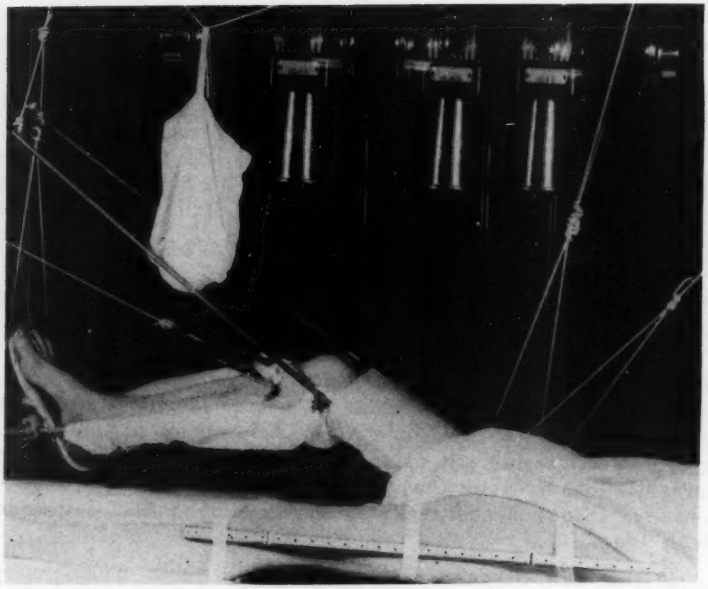

Figure 1.

Lottes *(5)* reported a method to be used at the patient's bedside. Two 10- by 12-inch cassettes and 2 medium Kirschner wires are used. One cassette is placed under the hip with the Kirschner wire under the greater trochanter and at a right angle to the long axis of the femur. The second cassette is placed below the first with the second wire parallel to the first and beneath the knee. The distance between wires is placed deliberately at 15 inches. One exposure is made over the trochanter and another over the knee joint. The length of the femur can be determined from the films by direct measurement of the distance of the upper wire from the tip of the trochanter and the distance of the lower wire from the knee joint. A direct measurement of the medullary canal on the film is used for the canal width.

(5) Lottes, J. O.: Treatment of fractures of femur with heavy, large cored, three-flanged medullary nail. Surgery 29: 868-884, June 1951.

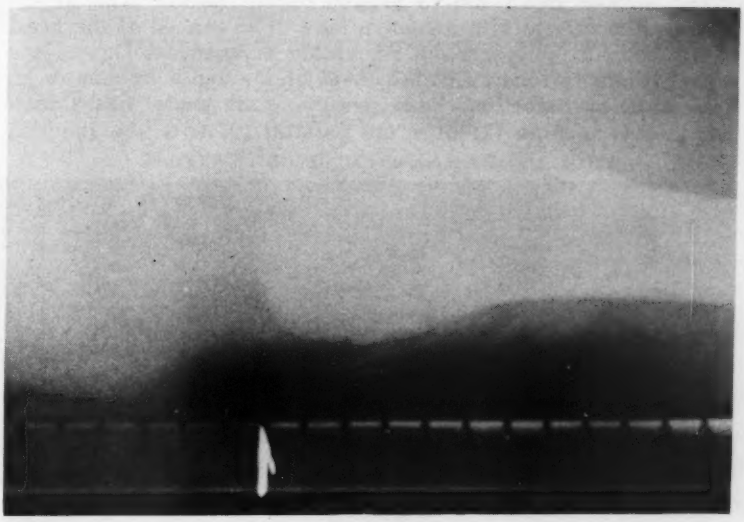

Figure 2.

METHOD

Our method uses the principle of Bell and Thompson *(4)* with some simplification. Like the method employed by Lottes *(5)*, the patient does not have to be moved to the roentgen table. In spite of this, it has proved to be very accurate. A metal rod with saw-cut markings at intervals of 1 cm. is used. Our rod is of ordinary bar stock aluminum found in most brace shops. Additional radiopaque markings made by wrapping wire about the rod at intervals of 40 cm. speed the calculations.

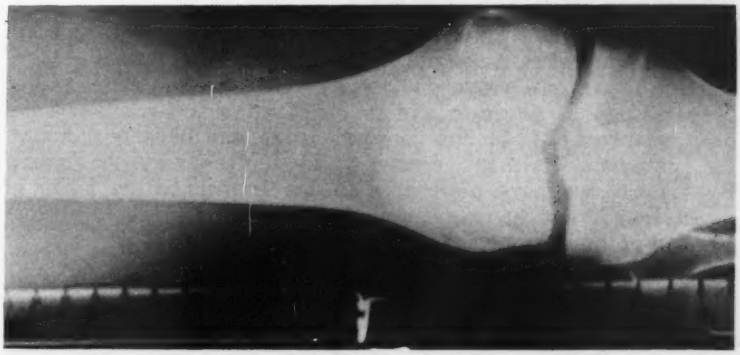

Figure 3.

The marked metal rod is affixed to the lateral side of the uninjured extremity with adhesive tape. It is placed at the level of the bone to help rule out projection differences. One of the wire markers is located at the level of the upper trochanter as determined by palpation. Roentgenograms are made with a portable x-ray machine (1) over the patella, (2) over the junction

Figure 4.

of the upper and the middle third of the femur, and (3) over the trochanter (fig. 1). On the roentgenogram, the relation of the wire on the metal rod above or below the trochanter (fig. 2) or condyles (fig. 3) is determined at a glance. The centimeter markings are easily read and the distance between wires, being 40 cm., enables one to calculate rapidly and accurately the length of the femur. The third film (fig. 4) is used to calculate the medullary canal width. A centimeter ruler is used to measure the narrowest portion of the femoral canal on the developed film and the length of the centimeter marking of the metal rod at the same level. The true width, ruling out projection differences, is calculated as follows.

If 1 cm. on the rod measures 1.2 cm. on the film, and the width of the canal measures 11 cm. on the film, $1.2/1 = 11/x$ where x is the true width, and $x = 9.16$ cm., the true canal width. This method is accurate and is simpler than others that have been advocated. It is not time-consuming and does not disturb the patient's fractured extremity by unnecessary movement. By its use we have been able to use intramedullary nails of exact length and have avoided, in many cases, the complications of painful pin bursas.

THE FORGOTTEN CALF

A Clinical Comment

WALTER R. MILLER, *Commander, MC, U. S. N. (1)*

THE title of this article was not prompted by a sense of facetiousness but rather by the idea of attracting attention to a badly overlooked subject. Rehabilitation of the musculoskeletal system following injuries has been emphasized since World War I and has been given great impetus during and since World War II. Orthopedists and general medical officers of all services have been made aware of the necessity for restoring the power of the quadriceps group of thigh muscles to near normal strength in the rehabilitation of injuries to the lower extremities. Great credit is due Thomas L. deLorme for his splendid work in developing passive resistive exercise to fit the particular needs of people with injuries to their extremities.

All persons engaged in the rehabilitation of patients with injuries to the lower extremities have been impressed with the fact that those with even severe injuries to the ligaments of the knee and residual relaxation and abnormal mobility in that joint can, if they have the will to do so, so develop the quadriceps group of muscles that their gait becomes almost completely normal. The knees of these patients become asymptomatic under even the conditions of military service.

For some strange reason it is common to see patients, who have had injuries to the leg, particularly in the lower half of the leg, and whose leg has been long encased in a cast, walk about the hospital and even returned to duty with an obvious flatfoot gait resulting in a limp and a list to the injured side with each step all because of failure to rehabilitate the posterior leg muscles which provide the strong, resilient plantar flexion of the foot and an adequate springy "take-off" with each step. Apparently it is easy to forget that when the ankle is immobilized in plaster, the muscles causing normal plantar flexion of the foot at the tibiotalar joint are not being used and therefore undergo rapid atrophy and diminution in size and power just as does the quadriceps group in the thigh when it is not being used. Furthermore, it also seems easy to forget that with fractures involving the leg, muscles of both the anterior and posterior compartment may become bound down in

(1) U. S. Naval Hospital, Portsmouth, Va.

the callus of the healing fracture and fail to function properly upon release of the leg from plaster.

Just as failure to develop the quadriceps muscles which stabilize the knee will result in a weak-knee syndrome with resulting long-continued swelling from joint effusion as an outstanding sign of instability, just so prolonged instability, pain, and effusion will be noted when the gastrocnemius-soleus complex is not rehabilitated following fracture. Just as in many cases diagnosis is made merely by thinking of the particular condition, just so the diagnosis of many flatfoot limps, noted long after fracture in the leg, can be readily diagnosed merely by viewing the calves of the two legs and noting the disparity in their size.

It is a simple matter to start the rehabilitation of this muscle group, if one remembers to do so. Tiptoe exercises wherein the patient rises up on the balls of both feet simultaneously performed along side of the bed for several minutes every hour of the day are excellent. At first the patient will carry most of the weight of the body on the unaffected side, being instructed gradually to shift more and more of his weight to the affected side until he is able to bear the full weight of the body when standing on the ball of the foot on the affected side for several seconds. He can then be started on an exercise which seems long to have been forgotten as a possibility in the hospital or even aboard ship but which requires no special equipment. This exercise, rope skipping, is well known to pugilistic trainers. A class can be started in this helpful exercise and most patients take part in it with enthusiasm especially if the instructor is able to introduce them to several fancy steps and call their attention to movie "shorts" of boxers in training camps where this method is used to bring the muscles of the lower extremity into condition. This not only develops the muscles of the leg, and particularly the plantar flexors of the foot and toes, but it also is an excellent method of completing the rehabilitation of quadriceps.

Too frequently a patient's rehabilitation consists of directing him to the physiotherapy department where he takes part in some rather dull, repetitious exercises once a day, following which he returns to his ward or to some working detail where he literally stagnates for the intervals between visits.

CONCLUSION

It behooves all of us to devise ways and means which will adequately rehabilitate patients for return to full duty, including combat by such methods as will require the least possible trained help. Recognition of the flatfoot gait due to atrophy of

the plantar flexors of the foot and toes in most cases can be readily accomplished by merely thinking of the condition in every patient in whom the lower leg and ankle are immobilized for periods greater than 3 weeks. Rehabilitation is easy if the patient is properly motivated.

BOOK REVIEWS

The Toxemias of Pregnancy, by *William J. Dieckmann,* S. B., M. D., Mary Campau Ryerson Professor and Chairman of the Department of Obstetrics and Gynecology of the University of Chicago; Chief of Service of The Chicago Lying-In Hospital and Dispensary; Attending Gynecologist, Albert Merrit Billings Memorial Hospital of the University of Chicago; Associate Editor of the American Journal of Obstetrics and Gynecology. 2d edition. 710 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publisher, 1952. Price $14.50.

Toxemias of pregnancy, due to their frequency and undetermined cause, remain the most important and confusing problem in the entire field of obstetrics. These complications occur in about 7 percent of all pregnancies, or in our country in about 140,000 annually. They account for a minimum of 1,000 maternal deaths and an estimated 30,000 stillbirths and neonatal deaths each year.

The format of this monograph is generally satisfactory, but the highly glazed paper reflects some objectionable glare especially under artificial lighting. Throughout the text, clarity is increased by the well-selected tables, graphs, drawings, and photographs. In the several summaries, the author's opinions appear to be impartial, although to a large extent based on personal observation. These views and conclusions are expressed in such a way as to stimulate interest and further investigative work for the purpose of confirming or refuting them. A sufficient number of key references to enable the reader to find others are cited.

The initial section deals with the history, classification, and pathology. The second section, on normal and abnormal physiology, includes an excellent chapter on physicochemical determinations, and the author substantially aids the reader by attempting to differentiate tests of theoretical interest and those of practical clinical use. In the discussion of the cause of eclampsia in the third section, the decreased function of the adrenal cortex with disturbance in sodium and water balances is suggested as a promising field for further investigation. In the

presentation of the clinical aspects of the toxemias in the next section, it is stressed that, because of the similarity of signs and symptoms, the differential diagnosis of true toxemia from the other types is difficult and depends on the past history, laboratory examinations, and the clinical course. Treatment is outlined and discussed in order to encourage rational management by selection of medications and procedures most appropriate for the individual patient after careful appraisal of the type and severity of the toxemia, response to medical treatment, and the existing obstetrical conditions. In addition to the analysis of the maternal and fetal prognosis, the final section discusses prenatal care which, intelligently rendered, can at least decrease the severity of these complications and thereby lower maternal and fetal morbidity and mortality.

As a result of a special interest in this obstetrical problem for nearly 3 decades, and the numerous reports of his clinical and laboratory studies, the author has become a recognized authority on the toxemias. He belongs to that school of thought which classifies at least half of the toxemias in the group wherein pregnancy is a complicating factor, intensifying the existing vascular or renal disease. He further believes that in most patients repeated toxemia represents the existence of prepregnant chronic vascular and/or renal disease and, only rarely, superimposed true toxemia or pre-eclampsia-eclampsia.

The excellent review and appraisal of numerous contributions pertaining to the physiology of pregnancy and the pathology and clinical aspects of toxemia, make this very readable monograph a valuable and interesting reference.

—Commander E. B. Hopper, MC, U. S. N.

Rare Manifestations of Metabolic Bone Disease, Their Practical Importance, by *I. Snapper,* M. D., Ph. D., Physician and Director of Medical Education, Mount Sinai Hospital; Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, N. Y. 29th Annual Beaumont Lecture. Delivered before the Wayne County Medical Society, February 6, 1950. 96 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $3.

This small book represents one of a series of lectures on the subject of metabolism, being essentially a condensation of the author's comprehensive: Medical Clinics on Bone Diseases (1949). After briefly reviewing present concepts of osteogenesis and calcium metabolism, he discusses the common and uncommon biochemical changes manifested by hyperparathyroidism and multiple myeloma. He then includes a short differential list of diseases affecting bone, urging that more care be given to exhausting the diagnostic possibilities. The student and busy practitioner will find this a clear, concise, ready reference on a somewhat obscure subject.

—Commander W. R. Miller, MC, U. S. N.

OVERSEAS RECEIVING AND RECOVERY WARDS

STEPHEN M. McCOY, *Major, MC, U. S. A.* (1)

EDWARD D. CAYIA, *Captain, MC, U. S. A.* (1)

WITH the passing of the years and the changing of personnel of the Army Medical Service, technics laboriously and painfully acquired in times of war are frequently forgotten. An example was the rediscovery in World War II of the technic of delayed primary closure of wounds which had been enthusiastically described in World War I. The loss, considered in terms of function of limbs and of the weeks needlessly wasted in treating war casualties by the closed plaster-vaseline gauze technic early in World War II, was truly incalculable. What is referred to is not the organic information found in manuals or directives, but the functional technics learned on the spot in practical application. Two aspects of the administration of a general hospital in a communications zone appear to belong in this category: the handling of convoys and the management of a recovery ward.

RECEIVING WARD

The familiar military phrase, "in accordance with the tactical situation," might appear to counsel against setting aside a portion of the available bed space for receiving patients by convoy. The number of beds required for a receiving ward will vary with the number of patients in the expected convoy and the time interval between convoys. At this 900-bed hospital it was found that an allotment of 50 beds was sufficient for this purpose. Patients were received by air evacuation and there was always adequate time for evaluation in the interval between convoys so that the receiving ward was not overcrowded.

On arrival, patients were put to bed and examined by a member of the admitting team on duty that day. Two admitting teams were constituted from the medical officers of all services in the hospital, each team being directed by a senior medical officer. Depending on the size of the convoy, the director called out 2 or more members of his team. In this manner, equitable rotation of this task was assured when convoys arrived during

(1) 343d General Hospital, Camp Drew, Japan.

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off-duty hours. This method released the professional officers of the day from a restricting duty, which often would otherwise have prevented their attendance on seriously ill patients elsewhere in the hospital. Also, 1 medical officer could not give adequate attention to the acutely ill patients of the convoy, review their battle tags, and write an intelligent admission note on 40 or even 20 patients. The time factor was important in that an experienced team of 4 medical officers could review a convoy in about 2 hours. During that period each patient was carefully examined, his dressings changed, and his records reviewed. Patients in the other wards had not been disturbed and the seriously ill patients of the convoy had been culled from the rest and earmarked for special nursing or professional care within a short time of their admission.

Ordinarily, convoy patients were retained on the receiving ward until after breakfast the next morning. The mess officer's task was made easier thereby because last-minute changes in food deliveries at breakfast were limited to the receiving ward.

Laboratory personnel were on hand when the convoy was admitted to draw blood for hemoglobin determination and hematocrit on all patients. If the hemoglobin was found to be below 10 grams, the examining physician was immediately notified, and crossmatching for transfusion was done. A urine specimen was obtained on each patient. The importance of this cannot be over emphasized because the cause of death in 2 of our patients was lower nephron nephrosis. Neither patient had been recognized as having lower nephron nephrosis prior to admission to our hospital. Although it is not implied that either death might have been prevented by earlier diagnosis, the responsibility for early diagnosis rests heavily on the medical officers attending the patient; and we believe that this type of screening can be done soonest and best on a smoothly running receiving ward.

Under normal operating conditions, all patients were received between the fourth and seventh day following injury. Débridement and primary care had been accomplished and most wounds were ready for reparative operation. In the receiving ward the chiefs of sections were able to examine and evaluate all admissions to their sections. This saved a large amount of walking about, searching for the new patients, and not a few unpleasant surprises. Often preliminary examination on the receiving ward enabled the chiefs or members of their sections designated by them to schedule patients for operation on the following day, or to order roentgenograms or laboratory procedures. In this way 24 hours were frequently clipped from the time required to obtain information vitally needed.

Consultations between sections and services were facilitated. Many hours were saved because representatives of the major services were on hand or on call for on-the-spot decisions rather than awaiting the lengthy process of submitting consultation requests.

RECOVERY WARD

A recovery ward is staffed by personnel trained in the problems of the immediate postoperative state and is equipped with aspirating machines, oxygen for nasal catheter and mask administration, a Levin suction apparatus, a Stedman pump, a bronchoscope, et cetera. All necessary medicines are also available.

With the advancement in surgical and anesthesiologic technics it has become evident that the reduction of patient morbidity and mortality depends on the treatment given during the period from the completion of the operation until the patient has regained his reflexes. In the immediate postoperative period hypoxia may appear by stealth if the respiratory airway is not carefully observed and maintained. The position of the patient may cause respiratory obstruction or embarrassment which may portend an atelectasis. Marked reduction in blood pressure may occur or a severe excitement state may result in injury. Dressings and casts applied tight enough to embarrass circulation may go unnoticed for hours unless trained personnel are alert to this possibility. Prolonged or shock-producing operations seriously weaken a patient so that further trauma in the immediate postoperative period might result in prolonged morbidity or even death.

The recovery ward should be adjacent to the surgery so that the patient does not travel a great distance in his depressed state. The surgery and the recovery ward must be considered an integral unit under the control of the anesthesiologist.

Depending on the daily operating schedule there should be one or more nurses in the recovery ward whose duties will be to care for the patients brought there, to give immediate supervision to the enlisted medical personnel, to administer medications, and to see that suitable charts are kept so as to reflect the patient's postoperative state while in the recovery ward. The enlisted personnel move patients from the litter to the bed, assist in positioning them in bed, and in moving them about. They can also be taught to watch the patients for signs of respiratory or other distress and to correct the condition or seek assistance. Proper functioning of the recovery ward depends on these enlisted attendants and every attempt must be made to instill in them confidence and pride in their work. They spell the difference between success and failure for the mission

of the recovery ward because there will be insufficient nurses to provide personal observation of all the postoperative patients. These men must be acutely aware of the tremendous value of their vigilance to the patient. One enlisted man in the recovery ward to each 2 or 3 patients occupying beds at maximum capacity is not excessive when considering the returns in health, time saved, and confusion avoided.

Transportation of the patient from the operating room to the recovery ward is by litter equipped with restraining straps. A Gatch bed is used if available. Suitable blocks or a chair are used to elevate the foot of the bed. A rubber sheet over the mattress and additional sheets and blankets are at hand to provide warmth if needed. An emesis basin, towels, and a drinking glass are contained in the bedside table, the top of which can be used to hold the patient's food tray. The enlisted attendants are taught to insert airways in patients with partial obstruction of the respiratory passages if positioning of the head is ineffective. A portable anesthesia machine is kept near the recovery ward to be used for maintaining artificial respiration on a patient whose lung excursions are shallow or have ceased. A positive-pressure resuscitator can be substituted if necessary. The personnel should know how to supply oxygen to the patient with either of these machines until additional aid is forthcoming.

A change of dressings is facilitated by the use of a wheeled dressing cart. It should be supplemented by a sterile pack containing syringes, needles, a knife, procaine, and epinephrine for emergency use in treating cardiac arrest. Another sterile pack should contain the bronchoscopes to be used for aspiration of the bronchial tree.

A standard stimulant tray found on all wards and containing aromatic spirits of ammonia, amyl nitrite, atropine, caffeine and sodium benzoate, injectable digitalis, epinephrine, metrazol, and nikethamide can be supplemented with apomorphine, sodium amytal or pentothal sodium, and picrotoxin. Fluids for parenteral use are stocked with suitable tubing. A sufficient number of fire extinguishers and hand litters for evacuating patients in case of fire must be available. The recovery ward is well placarded to keep the curious from trespassing and signs proclaiming the use of oxygen and prohibiting smoking are prominently displayed.

The depressed postoperative patient must be observed carefully until he regains consciousness or all his reflexes. To leave him in the care of untrained personnel can jeopardize his recovery. To place him on a large general ward in this condition

disrupts the normal routine unnecessarily, and the personnel may be too busy through sheer numbers of patients to supply the proper care. The use of a recovery ward results in economy of lives, health, time, and material.

BOOK REVIEWS

Diseases of the Chest, by *T. Royle Dawber,* A. B., M. D., F. A. C. P., Senior Surgeon, U. S. P. H. S.; Chief of Heart Disease Epidemiology Study, National Heart Institute; Assistant in Medicine, Harvard Medical School, and *Lloyd E. Hawes,* A. B., M. D., D. A. B. R., Radiologist at Faulkner Hospital; Consultant at U. S. P. H. S. Hospital, Boston. 440 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publisher, 1952. Price $10.

This book has the advantage of having been written by an internist and a roentgenologist in collaboration. The first 2 chapters offer a concise review of the elementary aspects of the anatomy, respiratory mechanism, and methods of study of the chest. A discussion of the chest wall from a roentgenologic standpoint follows. This excellent chapter describes common artefacts, congenital abnormalities, and bony lesions as seen in roentgenographic studies. Ensuing chapters cover diseases of the chest by organs involved in a manner which will be of the greatest value to the many doctors who must review numerous roentgenograms of the chest and treat varied chest diseases in the course of a busy practice. This book is not designed as an all-inclusive reference work. Technics are wisely omitted. The general medical and roentgenologic aspects of chest disease are well correlated. Of particular value are the innumerable hints on interpretation of roentgenograms recognizing the pitfalls of such interpretation. Diagnostic points which are not usually found in textbooks are mentioned for each disease. The author's style is simple and direct. The numerous illustrations of typical roentgenograms are very informative. The book is well bound and the paper is of high quality. An appropriate bibliography is included. It is believed that general practitioners, internists, and general surgeons will gain much useful information from this book.—*Lt. Col. B. A. Nichol, MC, U. S. A.*

History of American Psychology, by *A. A. Roback.* 426 pages; illustrated. Library Publishers, New York, N. Y., 1952. Price $6.

This is a compact, superbly written account of the principal events and trends out of which modern American psychology has been fashioned. It passes over the bulk of genealogic detail

which links our psychology with forerunning British and Continental European developments, that task having been accomplished by Boring. Instead, it directs attention to the scarcely explored pre-experimental epoch of the 250 years prior to William James' *Principles*. The impact of British and European traditions is seen largely through intimate accounts of such American teachers as Munsterberg, Titchener, Hall, and Cattell. Pre-experimental and experimental epochs in America are linked, and the ensuing developments are followed to the present day. A delightful authenticity pervades the book because the author's own professional life has overlapped those of the great figures of the American experimental period.

The book is divided into 4 parts. The first deals with the pre-experimental theologic orientation of psychology as taught at Harvard, Yale, Princeton, Columbia, and the University of Pennsylvania. Typical subject matter of the period is cited, prominent teachers are portrayed, and important books and publications are noted. Broad German and Scottish influences are elucidated. The second part covers the formative years of the experimental period, highlighted by the opening of laboratories throughout the East and Middle West. This part is by far the most rewarding, for it contains intimate personal views of the early great figures of the contemporary period. The third part traces the diversification of views culminating in the development of "schools." Part 4 views the various "branches" of effort, such as educational, applied, experimental, and physiologic, and offers a few speculations about the future. Scattered throughout the book are reproductions of what surely must be rare photographs of psychology's greater teachers.

This scholarly work is worthy of the attention of all psychologists, young or old, and it should be declared required reading for graduate students in psychology. It will appeal less to non-psychologists, largely because the author has left the telling of much important detail to other historians. Even the educated layman, however, will enjoy the often bold and witty reflections on the foibles of our early masters. The spectacle of Roback taking Boring to task in matters pertaining to the defense of their respective heroes is well worth the price of the book.

—*Major R. B. Payne, U. S. A. F. (MSC)*

AN IMPROVED APPARATUS FOR INTRA-ARTERIAL TRANSFUSION[1]

CARTER L. MEADOWS, *Major, MC, U. S. A.*

ROY L. ROBERTSON, *M. D.*

THE use of intra-arterial transfusion as a method of replacement therapy has become well established in the treatment of acute hemorrhage and traumatic shock. The principles underlying the use of this method and the experimental and clinical considerations have been dealt with in previous reports (2-6). Certain inherent advantages of the intra-arterial method over the conventional intravenous procedure merit consideration by the military surgeon.

Among these advantages are rapid restoration of both blood pressure and blood volume and immediate perfusion of the cerebral, coronary, and renal arteries under the desired pressure. In addition, the same volume of blood given by the arterial route appears to have an improvement factor of about 2 to 1 over intravenous replacement (7). Disadvantages include the necessity for special apparatus, the possibility of leaks or disruption of the apparatus under pressure, sacrifice of the artery following cannulation, danger of air embolism, and the possibility of tissue necrosis in the extremity subjected to prolonged infusion, unless it is periodically allowed to be perfused with oxygenated blood. This report will describe a modified apparatus which has several advantages over types previously used.

PREVIOUS METHODS

In the apparatus previously used for the administration of blood intra-arterially and intravenously under pressure, the

(1) From the Whitehead Department of Surgery, Emory University School of Medicine, Emory University, Ga.

(2) Seeley, S. F.: Intra-arterial transfusion in profound shock. Anesth. & Analg. 30: 195-210, July-Aug. 1951.

(3) Page, I. H.: On certain aspects of nature and treatment of oligemic shock. Am. Heart J. 38: 161-192, Aug. 1949.

(4) Glasser, O., and Page, I. H.: Prognostic signs in experimental hemorrhagic shock. Cleveland Clin. Quart. 13: 125-127, July 1946.

(5) Kohlstaedt, K. G., and Page, I. H.: Hemorrhagic hypotension and its treatment by intra-arterial and intravenous infusion of blood. Arch. Surg. 47: 178-191, Aug. 1943.

(6) Gold, I. B.; Rosenthal, J. L.; and Schotz, S.: Rationale of intra-arterial transfusion with case report. Anesth. & Analg. 28: 319-329, Nov.-Dec. 1949.

(7) Seeley, S. F.: Personal communication.

application of air pressure has been (1) either directly over the blood in the transfusion bottle or with the interposition of a small glass reservoir; or (2) from a cylinder of compressed air or oxygen, controlled by means of a reducing valve, as described by Ziccardi and Madden *(8)* and Porter et al. *(9)*.

Each of these methods has certain disadvantages. In the first instance, because the transfusion bottle provides a limited air reservoir, the passage of relatively small amounts of blood from the bottle into the patient's arterial system results in sudden and sharp drops in the air pressure over the blood. Constant vigilance is required on the part of the operator to maintain the desired pressure. In the second method, the use of compressed air or oxygen with reducing valves necessitates the transportation of heavy equipment with attendant inconvenience and expense; the reducing valves require constant regulation and repair; the continued flow of gas under pressure into the transfusion bottle may cause an explosion or other disruption of the system; and passage of an air bubble from the bottle into the artery may produce an air embolism.

The apparatus used until recently in the Emory University Hospitals, and previously described by Robertson et al. *(10)* was of the first type, in which air pressure is applied directly over blood in a small reservoir by means of a sphygmomanometer bulb. Experience showed that as the number of connections from glass to rubber were increased, the likelihood of leaks and disruptions of the apparatus and the consequent necessity for interrupting or discontinuing the transfusion likewise increased. Other modifications of the apparatus were therefore undertaken.

PRESENT METHOD

A large air reservoir in which air pressure could be applied directly over blood in the transfusion bottle was designed. The passage of a given amount of blood from the bottle would then cause a relatively small drop of pressure in the reservoir because of the disproportionate volumes of fluid and air. This was first accomplished by the use of a 1-gallon glass bottle. This was inconvenient because of the possibility of breakage and the danger of sudden rupture or explosion of the bottle while being subjected to air pressure.

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(8) Ziccardi, A. V., and Madden, J. L.: Apparatus for intra-arterial transfusion. Am. J. Surg. 81: 470-473, Apr. 1951.

(9) Porter, M. R.; Sanders, E. K.; and Lockwood, J. S.: Factor of rate of transfusion with particular reference to intra-arterial route. Ann. Surg. 128: 865-880, Oct. 1948.

(10) Robertson, R. L.; Trinchet, L. H.; and Dennis, E. W.: Intra-arterial transfusion; experimental and clinical considerations. Surg., Gynec. & Obst. 87: 695-704, Dec. 1948.

Accordingly, a modified form of the apparatus was constructed. A low metal stand with a plywood top was mounted on casters. An oblong steel tank, such as that used for surplus oxygen in aircraft, was placed beneath the top and anchored from above. A metal pump (bicycle or football type) was mounted in the frame adjacent to the tank and connected by a rubber tube and a nipple to the lower end of the pressure tank. The upper end of the tank has a T-connection from one end of which a short length of rubber tubing extends to an aneroid manometer

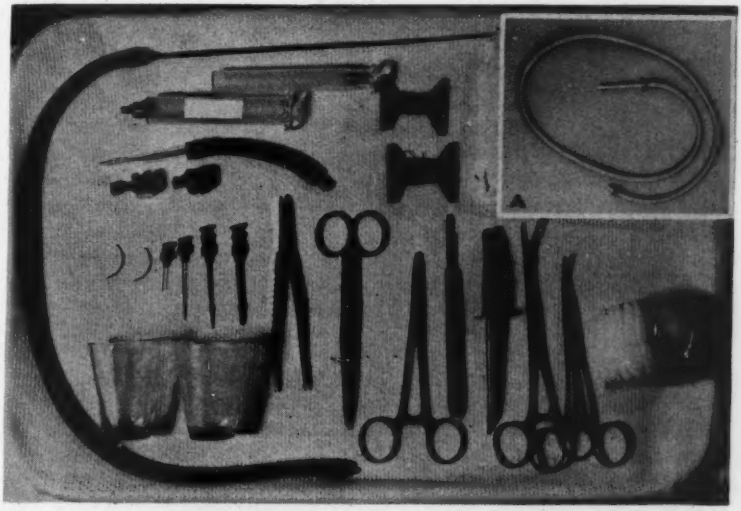

Figure 1. Contents of sterile arterial cannulation tray. Insert A shows slotted filter with rubber-tubing connection for very rapid administration.

which registers pressure. From the other end of the connection, a length of tubing extends for about 2 feet, at the end of which there is a small metal coupling which may be disassembled and which is identical with that used in sphygmomanometer cuff connections. The flat surface of the top of the stand provides space for the arterial cannulation tray and may be used for temporary storage of transfusion bottles or expendable plastic recipient filter sets *(11)*.

The sterile arterial cannulation tray (fig. 1) contains a syringe, hypodermic needles, medicine glasses for administration of local anesthesia if it is required to prevent arterial spasms, 2 metal cannulas (16-gage and 12-gage), one 12-gage glass

(11) These filters, which are adapted for use with pressure, may be obtained from the Baxter Laboratories.

cannula connected by rubber tubing to a needle adaptor, a scalpel, a slotted stainless steel filter with a short length of rubber tubing which is to be inserted between the plasma bottle and the expendable plastic recipient set, scissors, hemostats, forceps, pinchcocks, towels, gauze dressings, a long, large-bore plasma-aspirating needle with a length of tubing by which it is connected to the other half of the metal sphygmomanometer coupling and tube (through which air pressure from the reservoir is introduced over the blood), a needle holder, curved needles, and suture material.

Insert A shows a short rubber tube joined to the slotted stainless steel filter. When more rapid arterial transfusion is indicated, the plastic recipient set with its lengthy tube may be removed and the short tube connected directly with the cannula in the radial artery. By using this modification, blood has been delivered satisfactorily at the rate of 500 cc. in 1½ minutes, whereas twice that length of time is required to deliver the same amount of blood when the slotted metal filter and the plastic recipient set are used together. Although small particles theoretically can pass from the bottle to the patient by this means, we have not as yet had any such complications. Figure 2 shows the apparatus assembled and ready for use and figure 3 shows it in use.

Assembly of the apparatus and administration of the arterial transfusion can be quickly accomplished by a single operator. The assembled unit is rolled to the bedside or operating table, the sterile arterial cannulation tray is opened, and surgical exposure and cannulation of the selected artery is performed. The cannula is securely anchored in the artery with the end pointing proximally and the artery distal to the side of cannulation is ligated. Next, the plastic expendable recipient set is joined to the slotted filter and the filter is thrust into the thin portion of the rubber stopper of the transfusion bottle. The plasma needle is then pushed through the thick portion of the rubber diaphragm and its tube is coupled to that leading from the pressure reservoir under the table. The transfusion bottle is then inverted on a low hypodermoclysis stand. Pressure in the air reservoir is quickly raised by a few strokes of the bicycle pump, causing air to enter the transfusion bottle and to force blood out through the slotted filter into the recipient set and tubing. As soon as the tubing is completely filled and no air remains within the system, the stylet is removed from the cannula in the artery and the needle adaptor of the plastic transfusion set is inserted in its place. The transfusion is then ready for administration at the desired pressure and speed.

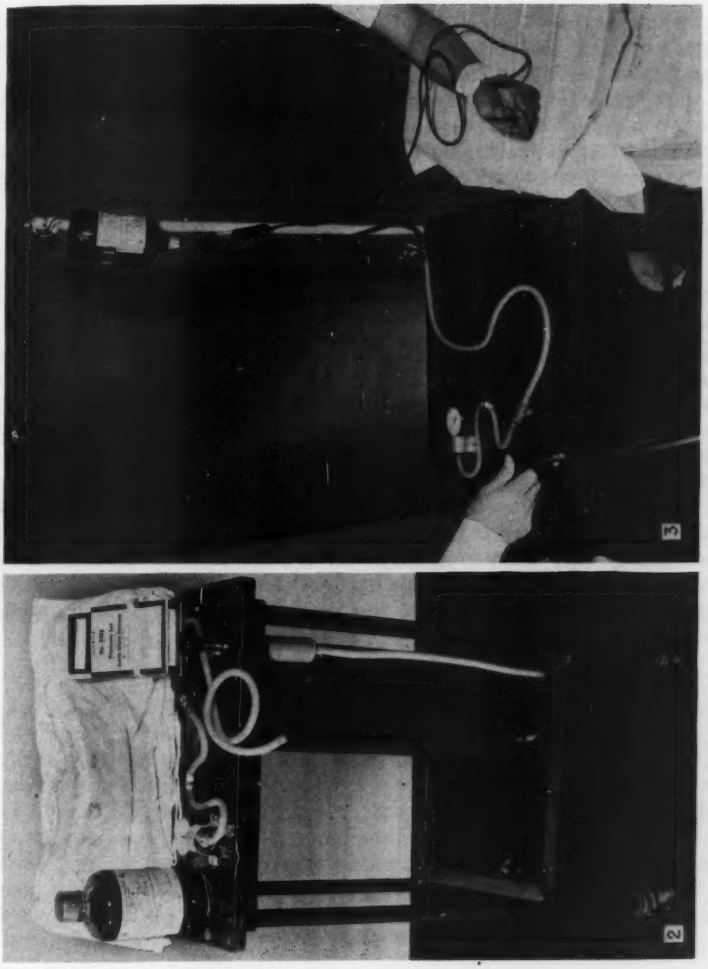

Figure 2. Apparatus assembled and ready for use. Figure 3. Apparatus assembled and in use.

As the transfusion bottle empties, care must be exercised to prevent air from entering the filter system and subsequently the artery and thus causing air embolism. When about 50 cc. of blood still remains in the bottle, preparations are made to exchange the bottle for a full one.

By placing a clamp across the tube leading from the pressure reservoir and removing the plasma aspirating needle from the transfusion bottle, equilibrium is reached between the pressure in the bottle and in the patient's artery, and a clamp is then placed across the tube leading directly to the patient. The slotted filter is removed from the depleted bottle and it and the plasma needle are both thrust into the top of the fresh bottle in the same manner used with the original container. This exchange can be accomplished in less than 30 seconds.

The *advantages* in using the described apparatus are: (1) the speed with which the apparatus can be assembled and blood can be delivered under pressure to the patient; (2) the rapidity with which an empty transfusion bottle can be replaced by a fresh one; (3) the ability of a single operator to assemble the apparatus and accomplish the transfusion; (4) the elimination, to a large extent, of the possibility of disruptions or leaks in the connecting tubing and apparatus; (5) the use of a relatively large reservoir of air to deliver pressure over the blood, assuring a fairly steady flow of blood at the desired pressure without the constant need for pumping; and (6) the relatively easy accessibility and inexpensiveness of the apparatus, the lightness and portability of the entire unit, and the fact that it can be assembled with sterile and unsterile parts and kept together as one unit.

PRIAPISM IN SICKLE CELL ANEMIA

BRUCE F. CHANDLER, *Captain, MC, U. S. A. (1)*

EMMET L. KEHOE, *Colonel, MC, U. S. A. (1)*

PRIAPISM is a condition of persistent and prolonged erection of the penis, unaccompanied by sexual desire, usually painful, and not relieved by intercourse *(2)*. The condition is not common but may arise from a variety of causes *(3)*. A very infrequent cause of priapism is sickle cell anemia. In a complete review of the literature Campbell and Cummins *(2)* found only 16 reported cases. They added 5 cases of their own collected over a period of 10 years. The following case is presented to emphasize that, in a Negro, the presence of priapism should direct attention to the possible diagnosis of sickle cell anemia.

CASE REPORT

A 23-year-old Negro was admitted to this hospital on 19 September 1951. While en route to his home on emergency leave, he stopped in this city to visit relatives. After a drinking party and following sexual intercourse, his penis remained in a state of persistent, painful erection. He sought medical help at a civilian hospital 12 hours after the onset and was transferred to this hospital 5 hours later.

On admission, he appeared in acute distress. His temperature was 100.4° F.; his pulse was 100; his respirations were 24; and his blood pressure was 170/80. His scleras appeared slightly icteric. Scars were noted on the ulnar aspects of both hands and on the lateral aspect of his left foot, where accessory or sixth digits had been removed when he was 2 years old. His heart was not enlarged but on auscultation a systolic murmur, grade 2 in intensity, harsh and scratchy in character, was heard best in the second intercostal space just to the left of the sternum and was transmitted to his neck and apical areas. His penis was erect and turgid, but was not warm to the touch.

His hemoglobin was 8.9; his erythrocyte count was 2,850,000, and his leukocyte count was 14,600, with 68 percent neutro-

(1) Walter Reed Army Hospital, Washington, D. C.

(2) Campbell, J. H., and Cummins, S. D.: Priapism in sickle cell anemia. J. Urol. 66: 697-703, Nov. 1951.

(3) Bailey, H.: Persistent priapism. Brit. J. Surg. 35: 298-303, Jan. 1948.

phils, 31 percent lymphocytes, and 1 percent eosinophils. Sickling of the red blood cells was noted on the differential smear. Urinalysis showed a 1 plus qualitative test for protein, about 7 leukocytes, and from 1 to 5 erythrocytes per high power field. The icteric index was 25. The total serum bilirubin was 1.6 mg. per 100 cc. The serologic test for syphilis was negative.

On admission, he was given 2 cc. (60 mg.) of papaverine hydrochloride intravenously, without relief of the erection, and 20 mg. of diethylstilbestrol intramuscularly. This was followed by 16 mg. of morphine sulfate and 0.4 mg. of atropine sulfate subcutaneously were given every 4 hours. These also gave him no relief. He was taken to the operating room 12 hours after admission and tetracaine hydrochloride spinal anesthetic was administered. Thirty minutes of spinal anesthesia failed to reduce the priapism and bilateral longitudinal incisions, 1 inch in length, were made in the corpora cavernosa near the base of the shaft of the penis. One hundred cubic centimeters of thick, dark, unclotted blood were removed and the organ became flaccid. This was followed by sustained hemorrhage of fresh arterial blood and by the time hemostasis was obtained with gelfoam gauze and suture ligatures, the organ was as erect and turgid as before.

Following the attempted surgical correction, treatment consisted of conservative measures. A total of 2,300 cc. of whole blood was given. Diethylstilbestrol, chloramphenicol, analgesic applications to the penis, and hot Sitz baths were also used. The penis slowly lost its turgidity and by 27 October, 46 days after the onset of the priapism, was completely flaccid. The patient was completely impotent for 4 months, but by March 1952, he was able to obtain a partial erection.

Urinalyses repeatedly showed proteinuria and failure to concentrate above 1.014 even after Fishberg tests. The patient's cardiac murmur was thought to be due to his sickle cell anemia. The percentage of sickled forms in the circulating blood, without the addition of anoxic factors, was as high as 24 percent, and persistent leukocytosis was noted.

DISCUSSION

Diggs and Ching (*4*), in a discussion of the pathology of sickle cell anemia, were the first to note any relationship between this disease and priapism. One of their patients had definite residual fibrosis after the acute penile engorgement had subsided. They believed that the cause of the priapism was thrombus formation caused by the interlocking of the elongated, sickled erythrocytes in the narrow vascular spaces of the penis.

(*4*) Diggs, L. W., and Ching, R. E.: Pathology of sickle cell anemia. South. M. J. 27: 839-845, Oct. 1934.

Getzoff *(5)* found that, in the period from 1936 to 1941 at the Charity Hospital of New Orleans, of 57,455 Negroes admitted, 65 had sickle cell anemia, 11 had a chief complaint of priapism, and only 3 had both. He postulated that the explanation for priapism in sickle cell anemia was the occurrence of venous congestion in the penis which lowered the oxygen tension, thus causing increased sickling which produced further stasis, more sickling, and eventual thrombosis and occlusion of the vascular channels for venous return. The blood was then pooled in the sinuses, which was conducive to more sickling and further persistent erection of the organ.

The onset of priapism is usually sudden and may occur at any age. The ages of the reported cases ranged from 5 to 33 years. Priapism may be the first complaint of a patient with sickle cell anemia *(5)*. The condition may occur spontaneously, or it may be initiated by sexual intercourse, but it then persists, as it did in this case, after sexual desire has been satisfied and is not relieved by further intercourse. It is usually painful and may be accompanied by fever and by difficulty in urinating. In contrast to the usual transitory erection, in true priapism only the corpora cavernosa become erect and the glans penis and corpus spongiosum penis are not involved *(6)*.

Treatment, as a rule, is prolonged. Both conservative and surgical means have been employed, usually with none of the measures meeting dramatic success. In the conservative sphere, local heat or cold, analgesic agents, general or spinal anesthesia, diethylstilbestrol, papaverine, anticoagulant therapy, antibiotics, rectal diathermy, and multiple blood transfusions have all been used. Surgical measures have included ligation of the dorsal artery of the penis, division or alcohol injection of the pudendal nerves, division of the ischiocavernosus muscles, simple needle aspiration of the corpora cavernosa, or their incision and drainage. The last two methods are the safest surgical procedures and have produced occasional successful results. Ordinarily the priapism of sickle cell anemia has required from 10 to 47 days to subside *(5)*.

Impotence follows priapism in many patients, especially when incision and drainage of the corpora cavernosa has been employed. Campbell and Cummins *(2)* stated that, of the 7 patients with priapism and sickle cell anemia in whom this therapy had been used, all became impotent. Our patient was, however, able to maintain a partial erection 6 months later.

(5) Getzoff, P. L.: Priapism and sickle cell anemia; report of 3 cases. J. Urol. 48: 407-411, Oct. 1942.

(6) Harrison, F. G.: Priapism; report of 3 cases. Pennsylvania M. J. 50: 1074-1077, July 1947.

"Cancer Cures" and Mr. Hoxsey's Nostrums

Physicians concerned with the welfare of the frequently misled public will be delighted at the recently ordered injunction against interstate shipment by Mr. Harry M. Hoxsey or the Hoxsey Cancer Clinic of "brownish-black, and pink, colored liquids intended for use in the treatment and cure of cancer in man." On 31 July 1952, the U. S. Court of Appeals for the Fifth Circuit, at New Orleans, reversed the judgment of the trial Judge of the U. S. District Court at Dallas, Tex., stating that, "The facts of the case require the issuance of an injunction, and the Court's failure to do so evidences an abuse of discretion."

Mr. Hoxsey's clinic had been shipping his medicines to osteopaths or directly to patients in many parts of the country. The liquids, intended for oral administration, contained potassium iodide and such items as clover blossom, alfalfa, and cascara sagrada. The District Court, in concluding that some cancer cures had been wrought by these mixtures, admitted the testimony of lay patients, unsupported by any proof that they had ever had cancer, to the effect that the Hoxsey medicines had cured them. The Circuit Court opinion, in reversing the judgment, laid down the following principles, based on testimony by cancer experts:

"* * * there is only one reliable and accurate means of determining whether what is thought to be cancer is, in truth and fact, actually cancer. This requires a biopsy, a microscopic examination of a piece of tissue removed from the infected and diseased region." "* * * the opinion of a layman as to whether he has, or had, cancer, or a like opinion as to whether he has been cured and no longer bears the disease, if, in fact, it ever actually existed, is entitled to little, if any, weight." "* * * despite the vast and continuous research which has been conducted into the cause of, and possible cure for, cancer the aggregate of medical experience and qualified experts recognize in the treatment of internal cancer only the methods of surgery, X-ray, radium and some of the radio-active by-products of atomic bomb production."

Unfortunately, the Hoxsey Cancer Clinic still flourishes unhampered in Dallas, Tex., so long as it keeps out of interstate commerce, but the action of the U. S. Court of Appeals gives hope that something effective may be done about the perennial rash of quack remedies for cancer with which the suffering public is bilked.

POSTOPERATIVE ACRYLIC PALATAL STENT

WILLIAM V. HILL, *Lieutenant Colonel, DC, U. S. A.* (1)

JOHN L. SOLIMINE, *Captain, DC, U. S. A. R.* (1)

LARGE areas in the palate devoid of mucoperiosteum following the surgical removal of tumors or following severe lacerations due to accidents often present a problem of postoperative management. Heat, cold, and the passage of food all contribute to the discomfort of the patient during the healing period. The relatively poor blood supply and nature of the tissue of some areas of the palate are not conducive to rapid healing. When electrocautery is used, healing may be further delayed. In the case here described, a palatal stent was used.

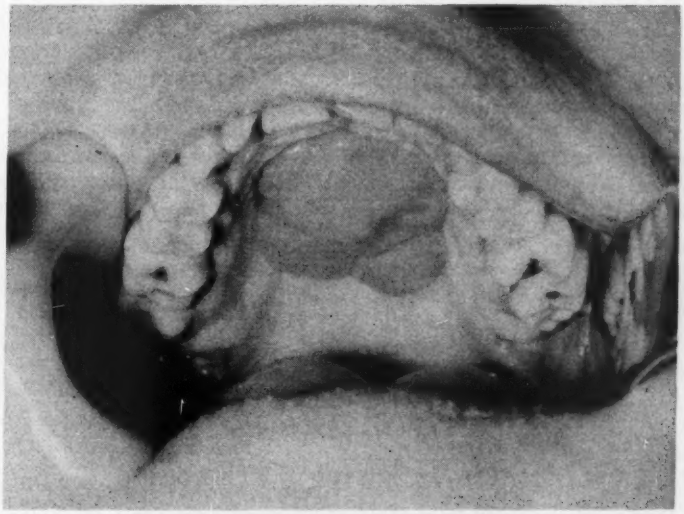

Figure 1. Tumor prior to excision showing 3 definite lobes.

CASE REPORT

A 23-year-old man was found to have a growth in the hard palate. This growth was lobulated, firm in consistency, pink, and attached to the palate with a broad flat pedicle. It measured 2.5 by 3.5 cm. and occupied about half of the palatal vault (fig. 1).

(1) Dental Clinic, Fort Monmouth, N. J.

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The patient stated that no one had discovered this growth on examination before, although he had known of its existence as long as he could remember.

Figure 2. Excised tumor showing severed pedicle.

The growth was surgically removed under local anesthesia (fig. 2). The pedicle was removed from the palate with a scalpel, leaving an area of denuded bone about 1.5 cm. in diameter, the mucoperiosteum being attached to the pedicle. The growth on microscopic examination was found to be a fibroma. Prior to operation an alginate impression was taken of the upper arch and an acrylic stent was constructed. In trimming the tumor area from the cast, a 2-mm. thickness was left in the pedicle area in order

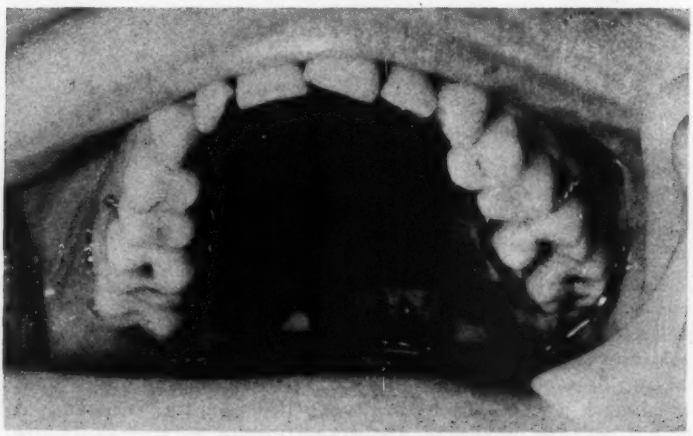

Figure 3. Acrylic palatal stent in place.

that a space of that thickness would exist between the finished acrylic stent and the pedicle area to be removed surgically. The remainder of the stent was to be in contact with palatal tissue.

The stent was prepared with holes in the interproximal space area of the first bicuspid and first molar area to allow for the passage of stainless steel wires to retain the appliance in the mouth (fig. 3). Following removal of the tumor, a cotton-waste dressing, saturated with balsam of Peru was applied over the denuded area. This was held in place by means of the stent and the dressing was retained for 48 hours, at the end of which time the balsam of Peru dressing was changed. This treatment was repeated for 10 days, by which time the denuded area was fully covered with tissue and well healed. At no time following the removal of the tumor did the patient have any discomfort. He was able to eat a normal diet. Cleansing washes after meals were unnecessary. The wound did not suppurate at any time.

The use of such appliances changes a normally painful, unpleasant, slowly healing wound to one which is painless, odorless, and rapidly healing and furthermore saves the time of both the patient and the operator.

BOOK REVIEWS

The Clinical Application of Antibiotics, Penicillin, by *M. E. Florey,* M. D., From the Sir William Dunn School of Pathology, Oxford. This volume, although a separate publication, is a continuation of the work described in **ANTIBIOTICS,** Volumes I and II, and may be read in conjunction with it. 730 pages; illustrated. Oxford University Press, New York, N. Y., publisher, 1952.

This authoritative and comprehensive work by one of the great pioneer investigators in the field of antibiotics will doubtless become the standard reference for all clinicians. After Sir Alexander Fleming's epoch-making discovery of the antibacterial properties of penicillin, it was Florey, along with Chain and others in England who did most of the original investigative work on the therapeutic properties of this invaluable drug.

The literature on antibiotics has grown tremendously in recent years. The bibliography alone in this book comprises about 73 pages and attests to the tremendous amount of preparatory reading done by the author.

The book is divided into 3 principal sections. The first is concerned with the properties of clinical importance and a general

consideration of the results of therapy; the second deals with the treatment of diseases due to specific organisms; and the third takes up the treatment of diseases considered by systems. The last section is of particular interest to medical officers because it includes an excellent chapter on the use of penicillin in battle casualties.

Unfortunately, in preparing a work of this magnitude, the time intervening between the review of the literature and the final publication is necessarily prolonged. Consequently, although the book was published in 1952, only the literature appearing up to the end of 1949 was considered. One suspects also that the chapters on rickettsial diseases and typhoid fever were written prior to the advent of chloramphenicol and terramycin because neither of these agents is mentioned in the text. Occasional mention, however, is made of aureomycin but not in these chapters.

The author has been scrupulously fair at all times in evaluating penicillin and has taken great pains to mention in the text any paper in which a well-based conclusion has run counter to the finding of most investigators. The chapters on the use of penicillin for infections within the thorax and for infections in infants are particularly well written and informative. This book should prove of unusual interest to all clinicians regardless of their specialties. Penicillin has proved to be of value in such a wide variety of medical and surgical conditions that it is difficult to conceive of a single medical specialty in which it has no place.

—Col. E. L. Kehoe, MC, U. S. A.

Living With Diabetes, by *Edward Tolstoi,* M. D. 90 pages. Crown Publishers, Inc., New York, N. Y., 1952. Price $2.

This monograph, written for the layman, is a lucid exposition of the author's thesis that diabetics should disregard sugar in the urine and should eat whatever they want, taking sufficient insulin to assure well-being and freedom from acidosis. It is unfortunate that the controversy between those who advocate "chemical control" and those who advocate "clinical control" diabetes should be presented to the lay reader. This monograph will result only in dissatisfaction and bewilderment of the diabetic patients of most of the physicians who follow the recommendations of the American Diabetes Association.

—Col. F. H. Mowrey, MC, U. S. A.

AGENESIS OF THE ILEUM AND JEJUNUM

HUGH P. CURTIS, *Captain, MC, U. S. A.* (1)

WILLIAM W. NICHOL, *Colonel, MC, U. S. A.* (1)

A CASE of agenesis of the ileum and jejunum recently seen at this hospital is of sufficient interest from a diagnostic and pathologic standpoint to include in the case reports of such abnormalities.

CASE REPORT

A 6-pound 1-ounce, full-term, male infant was delivered on 23 March 1952 of a 22-year-old mother, gravida I, Para 0, whose pregnancy had been uneventful and in whose family there was no history of congenital abnormality. Physical examination 8 hours after delivery revealed a slightly cyanotic infant who otherwise appeared perfectly normal. The patient was placed in an incubator and oxygen was administered shortly after birth and the cyanosis cleared about 9 hours later. Shortly after birth the patient vomited yellow material. He seemed hungry and attempted to eat but always regurgitated the food and water that was offered. This continued until 30 hours after birth, at which time it was noted that he had passed no meconium. A thermometer was inserted into the rectum and could be passed only about ¾ of an inch. A gelatinous white material was expressed from the rectum but no meconium was found. Rectal examination revealed a normal anus, but about 1 inch inside the rectum the finger was stopped by an obstruction.

Roentgenograms of the patient at this time showed dilated intestinal shadows which in the inverted position ended about 1 cm. proximal to the tip of a radiopaque instrument inserted into the rectum (fig. 1). The lateral view in this position showed the gas-filled loop of bowel to lie slightly anterior to the rectum. It was thought that the dilated bowel represented large bowel and that the patient had an atresia of the large bowel about 3 cm. proximal to the anus. An attempt to administer a barium enema was unsuccessful. The patient was prepared for operation and about 36 hours after birth his abdomen was explored through a left rectus incision under open drop ether anesthesia.

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(1) Army and Navy Hospital, Hot Springs, Ark.

A markedly dilated small bowel immediately filled the wound and exploration revealed that the small bowel ended in a blind pouch in the right lower abdominal quadrant with only a fine band connecting the terminal portion of the small bowel to the cecum which was about 1.5 cm. beyond the end of the small bowel. The cecum and entire large bowel was about 1 cm. in diameter and contained cheesy white material which could be moved through its lumen. The small bowel was much shorter

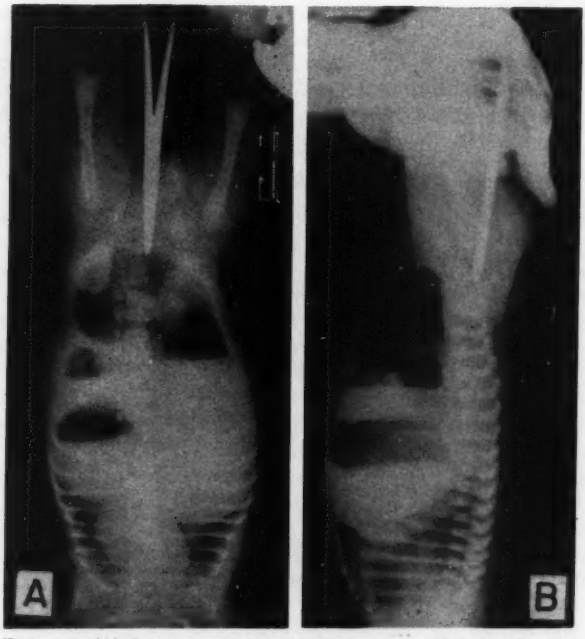

Figure 1. (A) *Posteroanterior roentgenogram.* (B) *Lateral roentgenogram. Note dilated loops of intestines.*

than normal. Saline solution injected into the mid-transverse colon was seen to dilate the colon proximally and distally. A side-to-side anastomosis between the end of the small bowel and the mid-transverse colon was performed using interrupted No. 0000 silk and continuous No. 0000 catgut on the posterior row, and a single layer of inverting Connell No. 0000 catgut sutures on the anterior row. The small bowel was opened proximal to the anastomosis following its completion and a catheter could be passed into the proximal and distal limbs of the large bowel. This opening was then inverted with two rows of sutures and attention was directed to the sigmoid colon which was about 1 cm. in diameter. Because the question of atresia of the rectum

was as yet unanswered, a loop sigmoid colostomy was performed and the wound was closed without event. The patient withstood the procedure well, receiving 45 cc. of whole blood and 350 cc. of 5 percent dextrose solution intravenously.

A small urethral catheter was inserted into his stomach preoperatively and was connected to Wangensteen suction apparatus postoperatively. Forty-eight hours postoperatively his colostomy was opened; a catheter was inserted into the colon proximally for irrigation; and 10 cc. of mineral oil was injected through the tube in order to dilate the large bowel and facilitate the passage of its contents. The patient was maintained during this time on intravenous fluids, penicillin, and streptomycin. On the fourth postoperative day hydration was excellent, he cried well, and was vigorous. The urethral catheter was removed from his stomach and he was given dilute glucose water by mouth. On the same day a small amount of green-black material passed from the tube in his colon and it was believed that the colostomy was functionally communicating with the small bowel. It was further noted that following instillation of mineral oil into his rectum, oil was obtained in his gastric aspiration. No more mineral oil was given by rectum.

On the fifth postoperative day small amounts of high protein, low-fat milk were added to his formula which he was offered every 2 hours. By the afternoon of that day he was vomiting intermittently and the urethral catheter was reinserted into his stomach. His formula was given through the urethral catheter, suction being applied to the catheter prior to each feeding. On the sixth postoperative day his weight was 5 pounds. He vomited a large amount of yellow material which was believed to be bile-stained milk curds. On the afternoon of that day he developed rapid and labored respiration with a temperature of 103° F. His color became ashen and he was seen to lie quietly in his incubator. Examination revealed numerous rales in both lungs. He was given 50 cc. of normal saline solution by intravenous drip and 30 cc. of whole blood by transfusion. His color remained waxy; his respiration became more labored; and he died.

On postmortem examination the lungs were red, firm, and did not float in water. On compressing them, a milky white mucoid fluid exuded from the surface. Microscopic examination revealed an extensive lobular inflammatory reaction which filled the alveolar spaces of the small bronchi with acute inflammatory cells and fibrin. The duodenum and the portion of the jejunum still present were partially dilated. The small bowel extended only 15 cm. beyond the ligament of Treitz, indicating agenesis of most of the jejunum and all of the ileum. The side-to-side anastomosis between the jejunum and transverse colon was intact. The colon had dilated to about 2½ times its size at the

time of operation. Water injected into the sigmoid colon was seen to pass out the anus, indicating that no atresia of the rectum was present. With the small bowel freed from the remainder of the abdominal contents it was seen to measure, from the pylorus to its blind ending, a total of 23 cm. against a normal of 350 cm. *(2)*.

Final diagnosis was (1) intestinal obstruction, due to agenesis of the ileum and most of the jejunum, with atresia of the connection between small and large bowel and (2) lobular pneumonia, secondary to aspiration of fluid.

COMMENT

The diagnosis of rectal atresia in this patient was based on (1) the presence of intestinal obstruction; (2) the apparent rectal obstruction, both to digital examination and to the attempted barium enema; and (3) more importantly, the roentgenographic findings of a dilated bowel which seemed to terminate just proximal to the rectum. Potts *(3)* has pointed out that positive differentiation of duodenal, ileal, and colonic obstruction is difficult in the infant because of the enormous dilatation, with the loops crowding one another into abnormal positions. The point might be made that in patients with suspected rectal atresia (type 4 of Ladd and Gross *(4)*), abdominal exploration is indicated to prevent an error in diagnosis such as was made in this patient. This would lend further support to Ladd and Gross' advice that these patients with type 4 rectal atresia should be treated by abdominal exploration and colostomy.

The actual pathology in this patient was agenesis of the major portion of the small bowel involving the entire ileum and nearly all of the jejunum, there being only 23 cm. of small bowel present as compared to the normal length of 350 cm. with an atresia of the connection between small and large bowel. From an anatomic standpoint a so-called microcolon was present, but, as pointed out by Lee and MacMillan *(5)*, microcolon is not a primary disease entity but is always secondary to proximal obstruction.

Atresias of the small bowel have been a highly fatal abnormality in the past. The survival rate depends to a large extent on the location of the atresias, those proximal to the ligament of

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(2) Watson, E. H., and Lowrey, G. H.: Growth and Development of Children. Year Book Publishers, Inc., Chicago, Ill., 1951.

(3) Potts, W. J.: Congenital atresia of intestine and colon. Surg., Gynec. & Obst. 85: 14-19, July 1947.

(4) Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood. W. B. Saunders Co., Philadelphia, Pa., 1941. pp. 25-43.

(5) Lee, C. M., Jr., and MacMillan, B. G.: Fallacy in diagnosis of microcolon in newborn. Radiology 55: 807-813, Dec. 1950.

Treitz having a more favorable prognosis than those distal to it *(6)*. This patient had agenesis of a large portion of the small bowel in addition to the atresia and, because of the agenesis, the condition was probably incompatible with life from a nutritional standpoint. The immediate cause of death was aspiration pneumonia, which accounts for a high percent of the deaths of infants with congenital abnormalities of the gastrointestinal tract.

(6) Rickham, P. P.: Neonatal surgery; early treatment of congenital malformations. Lancet 1: 332-339, Feb. 16, 1952.

BOOK REVIEWS

Applied Physiology, by *Samson Wright*, M. D., F. R. C. P., John Astor Professor of Physiology, University of London, Middlesex Hospital Medical School; Sometime Examiner in Physiology to the Universities of Oxford, London, and Leeds; The Royal College of Surgeons of England; The Royal College of Surgeons of Edinburgh; The Conjoint Board in England; The Conjoint Board in Ireland, with the collaboration of *Montague Maizels*, M. D., F. R. C. P., Professor of Clinical Pathology, University of London, University College Hospital Medical School, and *John B. Jepson*, M. A., B. Sc., D. Phil., A. R. I. C., Senior Lecturer in Biochemistry, Courtauld Institute of Biochemistry, Middlesex Hospital Medical School. 9th edition. 1,190 pages; illustrated. Geoffrey Cumberlege Oxford University Press, New York, N. Y., publisher, 1952.

Here is an old standby in a new, enlarged, and thoroughly rewritten and revised edition which is better than ever. As in the previous editions, Dr. Wright has produced a succinct, clear, and logical presentation of physiology which answers the questions posed by the investigator or practicing physician while fulfilling admirably its primary mission as a textbook. His method of writing in outline with short, terse statements and paragraphs facilitates the comprehension and use of current physiologic knowledge. The discussions of vomiting, defecation, and coitus are examples of the crisp manner in which Dr. Wright reviews a subject which is rarely taught as an organized whole, but is often asked in final or state board examinations.

Among the new features of this edition are: (1) the greatly increased number of illustrations, with a guide for their proper use; (2) the use of a professor of clinical pathology and of a senior lecturer in biochemistry as collaborators to give to physiology the unity it merits as a foundation for understanding medicine and surgery; and (3) an outline following the table of contents, which separates the preclinical material from that having mainly clinical

or specialist interest. Thus, the book can be as generalized or specialized as the user requires, yet still attain its avowed purpose of filling the needs and interests of both undergraduates and postgraduates.

It is difficult to find anything for adverse criticism except that the cover soils easily, and a general objection to the growing (and I fear unavoidable) bulk of all modern scientific texts. Fortunately, the author has not succumbed to the encyclopedic urge and the 2-column format presently so popular.

—*A. F. Lawton, M. D., Ph. D.*

Massage and Remedial Exercises in Medical and Surgical Conditions, by *Noel M. Tidy,* Member of the Chartered Society of Physiotherapy; T. M. M. G. 9th edition. 519 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1952. Price $6.

This book is written in the style of a "Merck Manual." Practically every disease entity or symptom complex known to medicine is discussed and physical treatment is recommended. Many of the statements are inaccurate, the discussion of disease processes is too brief to be of value; and the outlined treatment many times of no value or even possibly harmful.

This is the ninth edition of a book first published in 1932. With so many editions it is obvious that there has been considerable circulation. Apparently this book has been used extensively in England as a text for physical therapists. It might have some advantage to the senior physical therapy student who must have a broad but limited knowledge of many diseases in order to pass a final examination. This probably is the use made of this book in England.

From the standpoint of the American reader, I can see no value in this book. The physician interested in physical medicine has so much more accurate knowledge of disease processes than is presented here that his intelligence would be insulted by Tidy's approach. The training of physical therapists in this country is such that they would find the material as presented in this text juvenile and of little use either in passing an examination or treating patients.

It is regrettable that some previous reviews of this book have been so complimentary. I know of several physicians and therapists who have wasted good money in the purchase of this volume only to read a few pages and then put the book in the shelf never to open it again. Being one of those so taken in, I hope no one else will make the same mistake.

—*Lt. Col. J. N. Schaeffer, U. S. A. F. (MC)*

REPAIR OF CLEFT PALATE AND COLUMELLA WITH A TUBED SKIN PEDICLE[1]

JAMES CRAWFORD, *Commander, MC, U. S. N.*
CHARLES E. HORTON, *Lieutenant, junior grade, MC, U. S. N. R.*
RICHARD S. OAKEY, *Lieutenant, MC, U. S. N. R.*

THE cause, pathology, and treatment of harelip and cleft palate have been adequately presented by many authors and will not be included in this article. Although the employment of a tubed skin pedicle to close a cleft palate is not new (2-5), it is sufficiently rare to justify reporting the following case.

CASE REPORT

A 40-year-old woman who was born with a bilateral cleft of the upper lip and a complete cleft of the hard and soft palate (fig. 1) was not operated on for correction of the cleft lip until she was 4 years old. No further operation was permitted by the parents of the patient, although at the age of 16 she was fitted with a prosthesis to cover the palatal defect. Three infantile teeth appeared on her premaxilla, but these teeth were soft and loose and she removed them with her fingers. No permanent teeth appeared on the premaxillary portion of her alveolar ridge. By 1948, when she was about 37 years old, her prosthesis had extensively worn away the enamel on the existing upper teeth and she was advised by a dentist to discontinue the use of the artificial plate.

In January 1948 she entered a hospital elsewhere for closure of the cleft palate. Apparently because of the width of the cleft, it was deemed inadvisable to use the routine type of mucoperiosteal flap repair. Therefore a tube was constructed on the left side of

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(1) Plastic Surgery Service, U. S. Naval Hospital, National Naval Medical Center, Bethesda, Md.

(2) Blair, V. P.: Operative treatment of difficult cases of palate defect after infancy. Surg., Gynec. & Obst. 12: 289, 1911.

(3) Pickerill, P.: Facial paralysis, palatal repair and some other plastic operations. M. J. Australia 1: 543, 1938.

(4) Padgett, E. C.: Repair of cleft palates after unsuccessful operations, with special reference to cases with extensive loss of palatal tissue. Tr. Sect. Surg., General & Abd., A. M. A., pp. 336-358, 1929; also Arch. Surg., 20: 453-472, Mar. 1930.

(5) Thiersch, C.: Verschluss eines Loches im harten Gaumen durch die Weichtheile der Wange. Arch. d. prakt. Heilk. 9: 159-164, 1868.

her abdomen, transferred to her left wrist, and an attempt made to close her palate with this tube of skin, but after the tube was sutured to the edges of the palatal defect, infection occurred, and the distal one half of the pedicle was lost. In the process of constructing, delaying, skin grafting, and transferring the tubed pedicle 12 operations were performed.

Figure 1.

In October 1948, the remaining proximal half of the same tube was sutured on the mouth to close the palate, but the repair was lost when the pedicle was accidentally pulled loose while removing a Levin tube. This was the thirteenth operation in the attempt to close the palate. In November 1948, a second tubed pedicle was constructed on the right side of her abdomen and transferred to her right wrist, but the blood supply proved to be inadequate and this tube was lost. Twelve additional delaying and grafting operations were completed before the pedicle necrosed, making a total of 25 operations.

After the second pedicle was destroyed, construction of a third tubed pedicle was begun on her chest. In January 1950, before the third tube could be used, the patient's husband was transferred to another area and she reported to our hospital for further treatment. In the process of constructing the third tubed pedicle on her chest, 15 operations were required, making a total of 40 operations performed on the patient before admission to this hospital.

On admission to this hospital on 22 August 1950, physical examination revealed bilateral healed scars and an irregular mucocutaneous junction of the upper lip (fig. 2). The upper lip was small and was posterior in position and relationship to the nose and lower lip (fig. 3). Both alae nasi were wide and flaring, and

Figure 3.

Figure 2.

the tip of the nose was markedly depressed. The nasal columella appeared thin, scarred, small, and inadequate. There was a complete cleft of the hard and soft palate. Although the patient's vocal tones were typical of cleft palate speech, she had compensated remarkably for the defect. A tubed skin pedicle 6 inches long was present on her anterior chest wall. The distal end had been partially raised and a split-thickness skin graft applied. There were oblique, well-healed scars on the right and left side of her abdomen.

After a review of her history, it was decided that an attempt should be made to repair the posterior third of her palate by using double-ended mucoperiosteal flaps in the routine cleft palate closure. On 12 September this operation was performed and the flaps were approximated easily in the midline without undue tension, but postoperative separation of the anterior portion of the repair occurred until only 0.5 cm. of her palate remained united (fig. 4).

In December, a posterior pharyngeal flap with the base superior was raised and sutured to the nasal surface of the closed portion of her palate. This grew well, covering the posterior fifth of the cleft, and allowed her to close the posterior pharyngeal ring. A new prosthesis was obtained and although the patient's speech was improved, the obturator was not stable and the patient was not satisfied. Because the tube on her chest was in excellent condition and position it was decided to make an attempt to close the remainder of her palate with this tube.

On 31 May 1951 the tube on her chest was severed at its distal end. The edges of the skin flap were excised to fit her posterior palatal defect. The sides of her palate and the anterior portion of the pharyngeal flap were débrided and the raw surfaces of the skin flap, the palate, and pharyngeal flap were approximated with No. 00 chromic catgut sutures for a distance of 6 cm. around the circumference. The tube was of sufficient length to enable the patient to remain in a fairly comfortable position when the pedicle was brought into her mouth and sutured. She was fed by inserting a gastric tube through her mouth into her stomach. Further attachment of the tube to her palate bilaterally, closing the cleft except in the most anterior portion where there was no alveolar ridge, was accomplished in June.

On 7 July the proximal end of the tube was severed from her chest wall. On 18 July the scarred portion of her upper lip at its attachment to the columella was divided. The scarred columella was excised and the anterior end of the tube was brought out of her mouth above her upper lip. The upper surface of the tube was split and the skin trimmed so that the end of the pedicle would reach the tip of her nose without tension. The tube

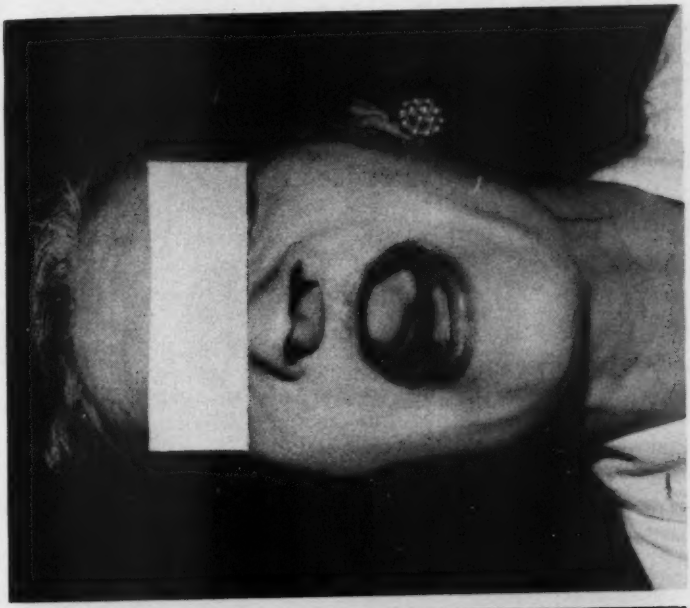

Figure 5.

Figure 4.

Figure 7.

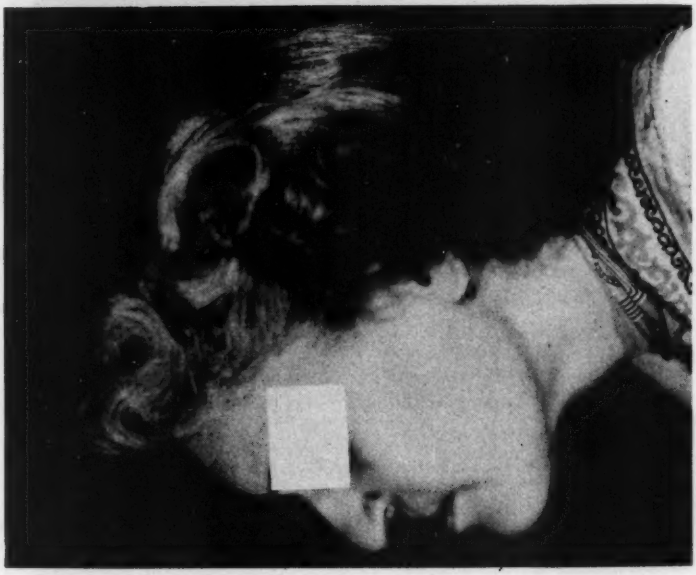

Figure 6.

was sutured to the dependent portion of the septum to form a columella of adequate length and width (fig. 5). This newly constructed columella required débridement of excess fat, which was done in October. Three weeks later her upper lip was pulled forward and attached surgically to the under surface of the recently formed columella. These operations resulted in an elevated nasal tip, a cosmetically acceptable columella, and an upper lip which was shifted forward and which appeared normal in position. Her oral and nasal cavities were completely separated anteriorly (figs. 6 and 7).

Figure 7.

For the first time she was able to eat and drink without the passage of food and liquid into her nose. Her speech was greatly improved and only a slight nasal tone remained. A few hairs are growing on the skin pedicle forming the palate but the tissue has adapted to the new environment without complications. A minor revision of the alae nasi was accomplished in November and a prosthesis to replace her missing upper teeth was obtained. No further operation should be necessary and the patient is at last free of her deformity. A total of 51 operations were performed before this result was accomplished.

It is not implied that the treatment of this patient should be standard for similar cases; rather, the failure of many commonly used surgical procedures is shown.

Figure 6.

BOOK REVIEWS

Textbook of General Surgery, by *Warren H. Cole,* M. D., F. A. C. S., Professor and Head of the Department of Surgery, University of Illinois College of Medicine; Chief Surgeon, Illinois Research and Educational Hospitals, Chicago, and *Robert Elman,* M. D., F. A. C. S., Professor of Clinical Surgery, Washington University School of Medicine; Assistant Surgeon, Barnes Hospital; Associate Surgeon, St. Louis Children's Hospital; Chief of Staff and Director of Surgical Service, H. G. Philips Hospital, St. Louis. Foreword by *Evarts A. Graham,* M. D., F. A. C. S., 6th edition. 1,154 pages; illustrated. Appleton-Century-Crofts, Inc., New York City, N. Y., publishers, 1952.

This new edition succeeds in adding to the fundamental surgical principles and practices presented in the outstanding fifth edition. The format is essentially the same and has been designed primarily for the student who is interested in gaining a basic knowledge of surgical diseases, their pathogenesis, and treatment. In order to cover adequately such a wealth of material, only well established principles have been included and these of necessity have been treated concisely and in a simplified way. An

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extensive bibliography, however, has been included. Major additions and revisions have been made in the presentation of chemotherapy, vascular surgery, endocrine diseases, thoracic and cardiac surgery, pre- and post-operative care, and massive gastrointestinal hemorrhage. The diagrams and photographs are plentiful and well chosen.

Nonoperative therapy is stressed with various surgical procedures mentioned but not described in detail because such information can better be presented in more specialized texts. The section on military surgery by Berry has been revised to include the changes that have developed from the most recent Korean experiences in organization, goals, and specific methods of transporting and treating patients. This portion of the book and those on intestinal obstruction, fractures, dislocations, and sprains are particularly well done. This book can be highly recommended to every physician who has any contact with the clinical practice of medicine. Although primarily designed for the student, the fact that each section is written by an expert in that field makes the book of value for all surgeons, whether recent graduates or experienced practitioners.

—*Capt. D. A. Baltz, MC, U. S. A.*

Skin Therapeutics, Prescription and Preparation (Materia Medica Dermatologica) by *M. K. Polano,* Head of the Dermatological Department, Municipal Hospital, the Hague (Netherlands) with an introduction by *Clarence S. Livingood,* Professor of Dermatology, the University of Texas, Galveston (Tex., U. S. A.). 276 pages. Elsevier Publishing Co., New York, N. Y., 1952. Price $6.50.

Except for a short historical introduction and some general considerations on dermatotherapeutics, this entire volume is devoted to a description of basic materials and their use in prescriptions for topical dermatologic therapy. Emphasis is placed on the selection of a vehicle for the dermatosis to be treated that will be pharmaceutically correct after the active ingredients have been added to it. Numerous sample prescriptions are given illustrating the use of basic materials as vehicles and as components in compound vehicles. These are usually followed by suggested combinations with specific remedies for use in the various dermatoses. The chapter on emulsions is presented with unusual clarity. The last 100 pages of the book consists of tables giving comparative lists of dermatotherapeutic drugs mentioned in the American, British, Swiss, and Dutch official formularies, with supplemental tables listing Belgian, Danish, French, German, Italian, Spanish, and Swedish dermatotherapeutic drugs. This last feature renders the book useful on an international scale as a formulary for dermatologic preparations.

—*Col. R. M. Williams, MC, U. S. A.*

MANAGEMENT OF CHEST INJURIES IN A MOBILE SURGICAL HOSPITAL

EDWARD E. ROCKEY, *Major, MC, U. S. A. R.* (1)

THE treatment of most of the thoracic injuries seen in a mobile Army surgical hospital (MASH 8076 AU) in Korea was conservative in contrast to that of the thoracoabdominal wounds which always required operation. A classification of the lesions is an aid in appraising the diagnostic and therapeutic problems. The injuries may involve the chest wall, the contents of the chest, or both.

CHEST WALL INJURIES

Stab and missile wounds of the chest need to be débrided, frequently under 1 percent procaine infiltration anesthesia. If there is a possibility of extension of the wound into the parietal pleura, it should be closed with interrupted No. 00 chromic catgut sutures up to the skin level.

Fractured ribs are evidenced by pain, mainly during the inspiratory phase of respiration. If roentgenograms of the chest confirm the diagnosis, the patients are treated by nerve block of the 2 intercostal nerves above and below the level of the fracture or fractures with 1 percent procaine.

Injury to an intercostal vessel causes a growing hematoma at the site of the chest wall wound and requires ligation of the torn blood vessel at the time of the débridement of the wound. In the area between the anterior and posterior axillary line of the chest wall where the vessels are located within a bony groove this cannot be done without resecting a segment of the rib.

Injury to an internal mammary vessel also causes a growing hematoma at the site of the chest wall wound near the sternochondral junction. The torn vessel is ligated at the time of the wound debridement.

INJURIES OF THE CONTENTS OF THE CHEST

Injuries to the contents of the chest in which the chest wall is apparently intact result from dull impacts to the chest. Patients with such injuries show varied evidence of respiratory

(1) Third Field Hospital, Korea, at time of writing.

distress depending on the extent of the injury and show signs and symptoms of pneumothorax, hemothorax, or hemopneumothorax. As soon as the clinical diagnosis is confirmed by posteroanterior and lateral roentgenograms of the chest, the blood and/or air is aspirated. This is repeated on the same day or daily until full re-expansion of the lung is accomplished. Frequently as much as 1,000 cc. of blood is aspirated at one time.

The aspirations are performed under aseptic conditions. In cases of hemothorax, under 1 percent procaine infiltration anesthesia, the intrapleural blood is first carefully localized by the insertion of a 20-gage needle at about the eighth intercostal space and midaxillary line. If blood is not obtained, an attempt is made at the anterior and posterior axillary lines and at higher levels. After the proper localization, a needle (not larger than 17 gage) is inserted and with the help of a 3-way stopcock and a 30-cc. syringe, the pleural space is aspirated as completely as possible. Prior to the withdrawal of the aspirating needle, 400,000 units of penicillin and 0.5 gram of streptomycin are instilled into the pleural space. In patients with hemopneumothorax or pneumothorax following the aspiration of the blood, the pleural space is also deflated. Unless the collapse is localized, the most advantageous site for the insertion of the aspirating needle is the second intercostal space at the midclavicular line. When possible, manometric readings are recorded and the air is aspirated by attaching the tube of a suction machine to the aspirating needle. The suction normally is maintained for as long as 15 minutes, which often results in complete re-expansion of the lung. If this procedure fails and the increasing subcutaneous emphysema suggests a continued escape of air, a thoracotomy tube (No. 24) is inserted into the pleural space in a dependent position for underwater drainage.

COMBINATION OF CHEST WALL WOUNDS AND WOUNDS OF THE VISCERA

The combination of chest wall wounds and wounds of the viscera of the chest are stab wounds and penetrating or perforating missile wounds. These result in hemothorax, pneumothorax, hemopneumothorax, and conditions requiring open thoracotomies.

Pneumothorax and hemopneumothorax may be associated with wounds of the open (sucking) or closed (tension) type. Patients with hemothorax, closed pneumothorax, and hemopneumothorax are treated by repeated aspirations and débridement of the chest wall wounds. The open wounds of the chest are treated under general endotracheal anesthesia. The wound is débrided, a thoracotomy tube is inserted through the débrided wound, and the blood is aspirated from the pleural space. The wound is then closed while the lung is kept inflated and the temporarily inserted thora-

cotomy tube is removed simultaneously. Frequently this technic makes added pleural aspirations unnecessary.

In those sucking wounds of the chest in which depressed rib fractures are present, the irregular rib ends are resected and the pleural space is irrigated with saline solution. Frequently a thoracotomy tube is inserted into the pleural space for underwater drainage. The chest wall defect is closed in layers by the approximation of the soft tissues outside of the parietal pleura with interrupted No. 0 chromic sutures. Attempts at closure of pleural tears are frequently impossible and unnecessary.

Conditions requiring open thoracotomy or its modifications include: (1) active intrapleural bleeding, (2) mediastinal perforation with injury or suspected injury to mediastinal structures, (3) the presence of large intrapleural foreign bodies, (4) wounds of the large bronchi or of the intrathoracic part of the trachea, and (5) wounds of the heart.

Active intrapleural bleeding results from massive lung laceration with or without intercostal or internal mammary vessel injury. The patient frequently is in shock. From 1,000 to 1,500 cc. of blood may be aspirated without changing the roentgenographic findings. Even though the patient is given more blood than the amount which is aspirated from the pleural space the hemoglobin and hematocrit levels remain below normal. At times, several pleural aspirations and repeated roentgenograms are needed to reach a definite diagnosis of active bleeding. In patients with clinical and roentgenographic evidence of massive hemothorax (frequently with bleeding and sucking chest wall wounds) and who do not respond to preoperative shock management, open thoracotomy should be performed without delay on the basis of suspected injury to a large vessel.

Mediastinal perforation with resulting mediastinal emphysema or perforation of mediastinal structures is another indication for open thoracotomy. In addition to the signs and symptoms of hemopneumothorax, patients with this condition present evidence of marked subcutaneous emphysema, particularly over the area just above the manubrium sterni. They are in much greater respiratory distress than would be expected from the extent of the existing pulmonary collapse.

Large intrapleural metallic foreign bodies are removed if they are easily accessible from the site of the entrance wound. These procedures are considered to be modified thoracotomies and consist of débridement of the entrance wound and its enlargement to a size sufficient to allow the insertion of the operator's hand into the pleural space. The metallic foreign body and loose bony particles are removed and the pleural space is evacuated and irrigated

with saline solution. Frequently a thoracotomy tube is inserted into the pleural space in a dependent position for underwater drainage. The chest wall wound is closed in layers.

Wounds of the large bronchi or intrathoracic part of the trachea are absolute indications for open thoracotomy. Patients with these conditions present evidence of hemopneumothorax with rapidly progressive subcutaneous emphysema. Needle aspiration or tube thoracotomy fail to re-expand the lung and ease the respiratory distress.

Wounds of the heart are easy to recognize if they present the classical signs of tamponade. Usually patients with this condition are in profound shock and in great respiratory distress. The heart sounds are muffled. The pulse is weak and thready and the pulse pressure is lowered. The problem is more complex when signs of cardiac tamponade are not present and the general condition of the patient is fairly good. In these patients, the location of the chest wall wounds and the estimation of the missile tract is of great help in the evaluation of the condition. If missile wounds of the heart are suspected, exploratory thoracotomy should be performed. Pericardial aspiration relieves patients with signs of cardiac tamponade. The xiphocostal is safer than the intercostal route for aspiration. Under 1 percent procaine infiltration anesthesia, a 19-gage needle is inserted at the left xiphocostal junction. The needle is directed at from 15 to 20 degrees to the left and upward and advanced posteriorly until the pericardium is perforated and blood is obtained.

OPERATIVE TECHNIC

Depending on the location and type of the injury, posterior, lateral, and anterior operative approaches are used for thoracotomy. The applicability of the anterior approach is emphasized. In this procedure, the skin incision extends from a point about 1 inch medial to the costochondral junction to the midaxillary line over the intercostal space at the desired level. This is frequently the third intercostal space in which case the third and fourth cartilages are divided. If added exposure is needed, the incision is extended downward at a right angle to its medial end and 1 or 2 additional cartilages are divided. The lung lacerations are débrided, the bleeding points controlled with No. 000 silk ligatures, severed bronchi are repaired or closed with No. 000 silk sutures, and the torn lung surfaces are approximated with No. 00 chromic mattress sutures. The visceral pleural edges are also approximated with No. 00 chromic catgut mattress sutures. Perforating missile wounds of the lung are similarly treated except that frequently gel foam strips are placed into the tunnel of the bullet tract prior to the closure of the entrance and exit wounds. Bleeding intercostal and internal mammary arteries are ligated. In pa-

tients with mediastinal emphysema, the mediastinum is drained. Perforated mediastinal structures are repaired. Cardiac wounds are approximated with interrupted No. 00000 twisted silk sutures. Intracardiac metallic foreign bodies are removed only if they are easily accessible. Following any of these procedures, the pleural space is carefully irrigated with saline solution. Two thoracotomy tubes are placed in the pleural space, one in a dependent position and one in the upper part of the chest for underwater drainage. The operative wound is closed in layers.

PREOPERATIVE AND POSTOPERATIVE CARE

Patients with chest wounds need to be evaluated as quickly as possible by careful inspection of the wounds, physical examination, and posteroanterior and lateral roentgenograms of the chest. Blood is given immediately to all such patients except those showing no evidence of appreciable blood loss. The tracheobronchial tree is kept as free as possible of blood and secretion by encouraging coughing and expectoration, bronchial catheterization, and, if needed, bronchoscopic suction. All the patients receive 1 gram of streptomycin and 1 million units of penicillin on admission, followed by 0.5 gram of streptomycin twice a day and 600,000 units of penicillin every 6 hours. This antibiotic regimen is maintained during their entire period of hospitalization. In the postoperative period, the patients perform breathing exercises which include guided deep breathing about 12 times each hour in addition to the use of a blow bottle. The patients with thoracotomy tubes have the benefit of frequent suction by a suction machine in addition to continuous underwater drainage. The thoracotomy tubes are removed within 48 hours except from patients with continued escape of air through the thoracotomy tube. In these patients, the tube is left in place as long as it is functioning. The patients are allowed up on the second and third postoperative day and evacuated in from 2 to 8 days.

CASE REPORTS

Case 1. Rupture of lung without chest wall injury. A 25-year-old man collided with a telephone pole, injuring the left anterior surface of his chest. On admission, he complained of severe pain in his chest dyspnea. Examination revealed marked tenderness over the upper anterior chest wall on the left side. A roentgenogram of the chest showed a 60 percent collapse of the left lung. Aspiration of 1,400 cc. of air from the left pleural space made him comfortable. Two days later, at the time of his evacuation, the lung had fully re-expanded.

Case 2. Injury to the chest wall and lung. A 22-year-old man was admitted 9 hours after he sustained a penetrating shell-fragment wound of the right side of his chest resulting in hemopneumo-

thorax. After 5 aspirations of blood and air, in 3 days he was evacuated. At that time he was asymptomatic and the lung was fully re-expanded.

Case 3. Open wound of the chest. A 21-year-old man sustained penetrating shell-fragment wounds of the left side of his chest and flank resulting in a sucking wound, a fragmented fracture of the seventh rib near the transverse process, and hemothorax. Under general endotracheal anesthesia, the wound was debrided; bony fragments were removed; the depressed uneven rib ends were resected; the pleural space was aspirated; a thoracotomy tube was inserted in a dependent position; and the wound was closed. Three days later, the thoracotomy tube was removed. Seven days following admission, the patient was evacuated with the lung fully re-expanded.

Case 4. Intrapleural metallic foreign body. A man sustained a penetrating shell-fragment wound of the right side of his chest. He was admitted 5½ hours after the injury with a sucking wound at about the seventh rib in the parascapular line. Roentgenograms showed evidence of hemothorax and a metallic foreign body which appeared to be in the pleural space. Under general endotracheal anesthesia, the entrance wound was debrided; the pleural tear was lengthened to 2½ inches; the foreign body was removed; and the pleural space was evacuated and irrigated. A thoracotomy tube was inserted in a dependent position and the wound was closed. Seven days later, at the time of his evacuation, the patient was asymptomatic, the wound healed, and the lung fully re-expanded.

Case 5. Active bleeding. A 19-year-old man sustained perforating bullet wounds of the left side of his chest. He was admitted in shock. The entrance wound was located at about the first rib at the midclavicular line and the exit wound at the seventh intercostal space in the parascapular line. Over the posterior chest wall, there was a rapidly growing hematoma the size of an infant's head and marked subcutaneous emphysema. A roentgenogram of the chest showed massive hemothorax. A large amount of bright red blood was aspirated from the stomach. Open thoracotomy was performed through the fourth intercostal space with the fourth, fifth, sixth, and seventh cartilages divided. Perforating bullet wounds of the upper and lower lobes of the left lung with the bullet tract extending from the apex of the upper lobe across the entire upper lobe to the apical segment of the lower lobe; fracture of the first rib anteriorly and the seventh and eighth ribs posteriorly near their transverse processes; and a tear of the seventh intercostal artery were found. The lung wounds were debrided; the bleeding points controlled with No. 000 silk ligatures;

the bullet tracts were cleansed with saline solution; and gel foam strips were inserted (4 into the upper and 2 into the lower lobe), and the entrance and exit wounds closed with No. 00 chromic mattress sutures. The torn intercostal artery was ligated. Blood from the pleural space was evacuated and the space was irrigated with saline solution. Two thoracotomy tubes were inserted into the pleural space and the wound was closed. The hematoma of the posterior chest wall was evacuated. The entrance and exit wounds of the chest wall were débrided and closed. The patient made an uneventful recovery and was evacuated on the sixth postoperative day. At that time he was asymptomatic and the lung was fully re-expanded. The roentgenogram showed only parenchymal clouding at the sites of the pulmonary wounds.

Case 6. Persistent bronchial openings. A young Colombian soldier sustained perforating bullet wounds of the right side of his chest. He was admitted in shock. The entrance wound was at about the fourth intercostal space at the posterior axillary line. The sucking exit wound was at the first intercostal space just mesial to the midaxillary line. A roentgenogram showed hemopneumothorax, fracture of the second, third, and fourth ribs, and metallic foreign bodies retained within the chest wall. After a 1,000-cc. blood transfusion, the wounds were débrided under general endotracheal anesthesia. The depressed irregular ends of the fractured ribs were resected; a torn axillary vein was repaired; 3 metallic foreign bodies were removed; a large amount of liquid and clotted blood was evacuated from the pleural space with the help of a tube temporarily inserted through the exit wound, followed by irrigation with saline solution and insertion of 2 thoracotomy tubes; and the wounds were closed. The 2 underwater-drainage tubes functioned well, but the patient became more and more dyspneic. On the next day a roentgenogram showed about 80 percent collapse of the right lung. At this time, open thoracotomy was performed through a posterolateral approach. About 1 cm. of the sixth, seventh, and eighth ribs was resected and the pleural space entered through the sixth intercostal space. A laceration of the upper lobe of the right lung, about 3½ inches long, was found extending from the lung surface to the hilum. Within the torn surfaces, there were numerous bronchial openings through which air was escaping freely. There was no active bleeding. The cut surfaces were débrided; the devitalized tissue was cut away; the bronchial openings were closed with No. 00 chromic mattress sutures; and the lung surfaces were approximated with No. 00 chromic interrupted sutures. The visceral pleural edges were approximated with No. 00 chromic mattress sutures. Seven days after the thoracotomy, the patient was evacuated in good general condition, his lung had re-expanded, and the wounds were clean and healing.

Case 7. Injury to the aorta. A young American soldier sustained multiple shell-fragment wounds of the left posterior portion of his chest. He was admitted in shock. He expectorated and vomited blood. He had a palm-sized, hissing, bleeding, soft tissue defect over the posterior chest wall, and marked subcutaneous emphysema. A roentgenogram showed clouding of the left side of the chest and depressed fractures of the seventh and eighth ribs posteriorly. The patient was given a 1,000-cc. blood transfusion prior to operation but his response was inadequate. His chest was entered through the sixth intercostal space. The lower lobe was indurated with blood, giving it the appearance of liver. A retained metallic foreign body was removed from this lobe. There was a bleeding opening over the upper mediastinal pleura. The pleura was opened at about the area of the active bleeding and the bleeding traced to the aorta at the level just below the arch. A metallic foreign body was partially covering a transverse tear of the aorta 1 cm. long at a point of its junction with an intercostal artery. The shell fragment was removed, and the bleeding controlled by approximating the tear with Allis' forceps. The tear was sutured with No. 00000 braided silk. At the conclusion of the repair, cardiac standstill occurred. The pericardium was opened. An intracardiac transfusion was given and cardiac massage was maintained for 30 minutes, but the patient died.

DISCUSSION

Early re-establishment of as normal a cardiopulmonary function as possible gives gratifying results. This was well demonstrated by the dramatic improvement of the general condition of the patients with sucking wounds, even those following the temporary sealing of the chest wall defects. The value of conservative treatment of chest injuries is well established (2-6). Repeated and early aspiration is the procedure of choice in most patients with hemothorax or hemopneumothorax. Sucking wounds are treated under general endotracheal anesthesia. Under these conditions a complete evacuation of the pleural space, adequate re-expansion of the lung, and clearing of the bronchial tree can be accomplished. Few of these patients need subsequent aspirations. The indication for open thoracotomy among battle casualties are few because bleeding from most pulmonary wounds becomes self-con-

(2) Mackler, S. A.: Experience with thoracic and thoracoabdominal wounds in evacuation hospital. J. Thoracic Surg. 16: 538-570, Oct. 1947.

(3) Woodruff, W.: Chest injuries. New York State J. Med. 48: 1142-1147, May 15, 1948.

(4) Snyder, H. E.: Management of intrathoracic and thoracoabdominal wounds in combat zone. Ann. Surg. 122: 333-357, Sept. 1945.

(5) Walsh, W. E.; Stubenbord, J. G.; and Tawse, R. W.: Penetrating wounds of chest. Am. J. Surg. 80: 176-182, Aug. 1950.

(6) Rockey, E. E.: Care of thoracic and thoracoabdominal wounds in combat zone in Korea. To be published.

trolled and only a few of those with active bleeding from the lung, large vessel, or the heart reach the hospital alive. Perforation of the diaphragm or its likelihood is an indication for laparotomy rather than for thoracotomy *(7)*. An anterior approach for thoracotomy *(6)* is favored because this is the quickest way of entering the chest and it gives adequate exposure. A careful closure in layers assures good healing of these wounds.

(7) Rockey, E. E.: Management of thoracoabdominal injuries at Mobile Army Surgical Hospital level in Korea. To be published.

BOOK REVIEWS

Normal Blood Pressure and Hypertension, New Definitions, by *Arthur M. Master,* M. D., Cardiologist, The Mount Sinai Hospital, New York; and Associate Clinical Professor of Medicine, Columbia University, New York, *Charles I. Garfield,* M. D., Research Assistant in Cardiology, The Mount Sinai Hospital, New York, and *Max B. Walters,* M. D., F. R. C. P. (CAN.), Member, Heart Station, Vancouver General Hospital, Canada; Formerly Research Assistant in Cardiology, The Mount Sinai Hospital, New York. 144 pages; 36 illustrations. Lea & Febiger, Philadelphia, Pa., publisher, 1952. Price $4.

This handbook on blood pressure, replete with historical background, discussion, and statistical data, attempts "to establish the true normal limits of the blood pressure." The normal limits proposed are the result of a statistical study of the blood pressures of 74,000 unselected, working people, ranging from 16 to 65 years of age.

The new range of normal blood pressure proposed by the authors is somewhat higher than those now commonly accepted and varies with age and sex. As an example, the stated range of normal systolic pressure of men from 20 to 25 years old is from 105 to 140, whereas the range in the same age group for women is stated to be from 100 to 130. The lower limit of hypertension for this age group is regarded to be 150 for men and 140 for women. In men from 50 to 55 years old the range of normal systolic pressure is stated to be from 110 to 160, whereas for women it is from 110 to 165. The lower limits of hypertension in this age group is regarded to be 175, for men and 180 for women. There is further variation to be considered for weight and physical condition.

The authors also make the plea to consider the proposed new limits of blood pressure merely as one factor in a whole picture, stating that blood pressure itself is only a symptom to be evalu-

ated in the presence or absence of associated and related clinical findings. Although acceptance of the proposed new standards will undoubtedly be somewhat slow, this effort is distinctly a step in the right direction and the proposals made could well be adapted to Armed Forces physical standards.

—*Col. C. L. Leedham, MC, U. S. A.*

Rorschach's Test, III. Advances in Interpretation by *Samuel J. Beck*, Ph. D., Institute for Psychosomatic and Psychiatric Research, Michael Reese Hospital, Chicago; Departments of Psychology, University of Chicago and Northwestern University. 301 pages. Grune & Stratton, Inc., New York, N. Y., publishers, 1952. Price $5.50.

This volume is a challenging, stimulating, and thought-provoking continuation of the author's studies on Rorschach's test. It contains the fruit of 5 years of research carried on under grant from the National Institutes of Health, and provides what the title promises—advances in interpretation.

Seven Rorschach records on 4 patients, either in analysis or therapy, are presented in detail. These broadly cover the years of childhood, adolescence, and young adulthood with the Rorschach test material being generously supplemented by data from the social worker's and psychiatrist's files. The end result is a contribution to the literature which is well worth the reading by anyone whose work involves a psychotherapeutic relationship with patients.

The objective, scientific, and yet intuitively sensitive manner in which Dr. Beck approaches and treats the dynamic material which is revealed by this projective psychologic test, and the manner in which he appraises the test itself is refreshing. He notes at one point: "We do have a good test, one that uses a fixed set of stimuli, and that gives results useful to the clinic and to the practitioner. Within a range of error moderate for what it attempts, the test provides dependable diagnostic pictures and guide posts for treatment. The test and its claims are now being subjected to some hard thinking and experimental check ----I look for hypotheses and a logic that will advance a science of the whole human personality. Whether this will be with the Rorschach, or any other test, will not then matter. Meanwhile, and in absence of research more convincing toward refuting the validities that have emerged, there are still the ten Swiss ink blots."—*Commander W. R. Griswold, MC, U. S. N.*

CONGENITAL ATRESIA OF THE SMALL INTESTINE

LOWELL R. STEELE, *Lieutenant Colonel, MC, U. S. A. (1)*

CONN L. MILBURN, Jr., *Colonel, MC, U. S. A. (1)*

ALTHOUGH congenital atresia of the small bowel occurs in only 1 of every 1,500 *(2)* to 20,000 *(3)* newborn infants, we must be constantly on guard to recognize its occurrence early, if the infant's life is to be saved.

Etiology. Intestinal obstruction in the newborn may result from either an intrinsic or an extrinsic lesion. An intrinsic obstruction is a defect in the continuity of the lumen of the bowel due to an intra-intestinal development error. Extrinsic obstruction is the occlusion of the lumen of the bowel by external pressures. Whether from intrinsic or from extrinsic cause, total intestinal obstruction produces the same clinical findings and the treatment and outcome are much the same.

Congenital intrinsic atresias of the small intestine are believed to be the result of an arrest in the embryologic development. Patten *(4)* stated that prior to the fifth week of fetal life, the intestine is a primitive tube with a lumen lined with epithelium. After the fifth week, the epithelium proliferates to an extent that the entire lumen of the small intestine becomes obliterated with epithelial concrescences. Thus, at about the eighth week, the intestine becomes a solid cord without a lumen. Sometime later, probably between the eighth and twelfth weeks, the diameter and length of the intestine increases so that the epithelial overgrowths spread out producing a vacuolation effect. As the diameter of the intestine continues to grow, the vacuole spaces coalesce to re-establish the intestinal lumen. An arrest in development during the "solid" stage results either in atresia or stenosis. Other theories of causation are fetal peritonitis *(5)* and vascular changes *(6)*.

(1) Letterman Army Hospital, San Francisco, Calif.

(2) Evans, C. H.: Atresias of gastrointestinal tract. Internat. Abstr. Surg. 92: 1-8, Jan. 1951.

(3) Webb, C. H., and Wangensteen, O. H.: Congenital intestinal atresia. Am. J. Dis. Child. 41: 262-284, Feb. 1931.

(4) Patten, B. M.: Human Embryology. The Blakiston Co., Philadelphia, Pa., 1946.

(5) Savariaud: L'occlusion congenitale interne. Rev. d'orthop. 2: 305, 1903.

(6) Theremin, E.: Ueber Congenitale Occlusien des Dunndarms. Deutsche Ztschr. f. Chir. 8: 34, 1877.

Pathology. Atresia of the small intestine is single in 85 percent of cases and multiple in the remaining 15 percent *(3)*. The lesion may be in the form of a single veil or diaphragm that blocks the lumen, but this type is the least common. The other form of atresia represents a congenital aplasia of a segment of bowel, the intestine ending in a blind sac. In some cases, the segments of bowel may be connected by a fibrous band *(7)*. With atresia the proximal portion of the bowel is greatly distended with gas and fluid (4 to 6 cm. in diameter) and the distal portion is collapsed (about 0.5 cm. in diameter). Due to the intraluminal pressure in the distended proximal portion, the walls become ischemic and necrotic. Ladd and Gross *(8)* stated that there is always danger of perforation after the third day of life in patients who are not operated on. The most common sites of atresia of the small bowel are (1) the ileum and (2) the duodenum. Of 47 patients observed by Ladd and Gross, 36 were in the ileum, 5 in the duodenum, and 6 in the jejunum. Davis and Poynter *(9)* collected 286 cases. Of these, the atresia was in the ileum and jejunum in 161 and in the duodenum in 134. Tandler *(10)* found in his series of 88 cases that the obstruction was in the ileum and jejunum in 55 and in the duodenum in 33.

Prognosis. Miller *(11)* pointed out that prior to 1911, there were no reported cases of survival from this condition. In that year, Fockens *(12)* reported the first successful treatment following lateral intestinal anastomosis. Survivals remained rare until recent years. Potts *(13)* stated that 20 years ago, a postoperative recovery was of sufficient rarity to be worthy of publication. Of the 47 patients operated on by Ladd and Gross *(8)* only 7 recovered. Today the mortality figures are constantly improving because of earlier diagnosis, chemotherapy and antibiotics, improved surgical technics, and better preoperative and postoperative management. The following is a case reported, not because of its rarity, but for the purpose of re-emphasizing the importance of the 4 cardinal factors in the successful treatment of such patients; namely, early diagnosis, preoperative care, prompt surgical treatment, and postoperative care.

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(7) Arnheim, E. E.: Surgery of newborn. J. Mt. Sinai Hosp. 17: 528-551, Mar.-Apr. 1951.

(8) Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood. W. B. Saunders Co., Philadelphia, Pa., 1941.

(9) Davis, D. L., and Poynter, C. W. M.: Congenital occlusions of intestines; with report of case of multiple atresia of jejunum. Surg., Gynec. & Obst. 34: 35-41, Jan. 1922.

(10) Tandler, J.: Zur Entwicklungs geschichte des Menschlicken Duod. in fruhem Embruonal stadien. Morph. Jahrb. 29: 187, 1902.

(11) Miller, E. M.: Bowel obstruction in new born. Ann. Surg. 110: 587-605, Oct. 1939.

(12) Fockens, P.: Zentralbl. f. chir. 38: 532, 1911.

(13) Potts, W. J.: Congenital atresia of intestine and colon. Surg., Gynec. & Obst. 85: 14-19, July 1947.

CASE REPORT

A 5-day-old girl was transferred to this hospital from an outlying hospital on 4 December 1951 with symptoms of intestinal obstruction. She had appeared normal at birth, but 3 or 4 hours later she began to regurgitate small amounts of clear fluid. The oral feedings given during the first 4 days of life were also regurgitated, the color of the vomitus becoming green brown. She had passed only a small amount of thin, yellow-green stool. Her fluid intake had been maintained by parenteral fluids.

On admission to this hospital she appeared remarkably well. Because she had received parenteral fluids, her hydration was good, and there were no findings indicating electrolyte or acid-base imbalance. Her abdomen was moderately distended and tympanitic. No bowel sounds were noted by auscultation. No meconium was present in the rectum. Her erythrocyte count was 5,020,000; her hemoglobin was 14.1; her leukocyte count was 12,550 with 45 percent neutrophils, 25 percent lymphocytes, 26 percent monocytes, 3 percent eosinophils, and 1 percent basophils; her nonprotein nitrogen was 38 mg. per 100 cc.; her chlorides were 110 milliequivalents per liter; her sodium was 143 milliequivalents per liter; and her carbon dioxide combining power was 17.5 milliequivalents per liter. A roentgenogram of the abdomen and a barium enema (figs. 1 and 2) revealed an obstruction of the small intestine, probably in the lower jejunum or upper ileum.

Preoperative measures designed to put the infant in optimum condition included decompression of the stomach and the administration of parenteral fluids and whole blood, penicillin, streptomycin, and vitamin K. Twenty-four hours after admission, the infant's condition was considered to be excellent, and she was taken to the operating room.

The peritoneal cavity was opened through a right rectus incision under open drop ether anesthesia. Exploration revealed that the duodenum and the proximal two-thirds of the jejunum were distended to 3 or 4 cm. in diameter. At about the junction of the middle and lower thirds of the jejunum, the bowel terminated in a blind pouch. At this point there was complete interruption of the jejunum and its attached mesentery, representing congenital segmental aplasia. The small intestine distal to this point was found to be collapsed and measured from 0.5 to 1 cm. in diameter. It was completely unattached to the proximal bowel (fig. 3). Saline solution was injected into the lumen of the distal segment of bowel through a small caliber needle, and the patency of this portion of the intestine was determined by observing the

Figure 1. Roentgenogram showing dilated stomach and multiple segments of distended bowel. Figure 2. Barium enema showing normal large bowel with reflux into ileum and dilated segments of small bowel.

passage of the fluid into the lower colon. A side-to-side anastomosis of the jejunum was completed using the technic recommended by Ladd and Gross *(8)* (fig. 3).

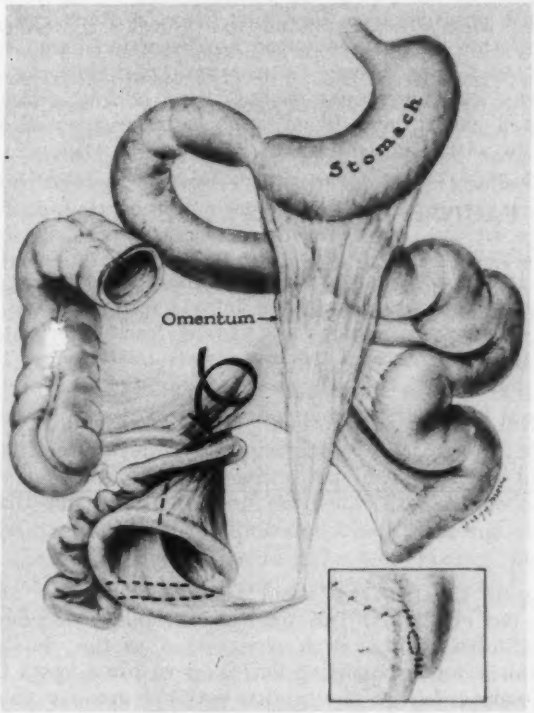

Figure 3. Diagram showing findings at operation. Note interruption of the small bowel continuity by complete absence of bowel and mesentery. The duodenum and proximal 2/3 of jejunum are distended and the distal 1/3 of jejunum and ileum are collapsed. Insert shows side-to-side anastomosis of jejunum.

Postoperatively, penicillin and streptomycin were given intramuscularly. Continuous gastric suction was maintained for the first 48 hours without oral feedings. Fluids, electrolytes, and whole blood were administered through an ankle vein. When the passage of small meconium stools occurred at the end of the second postoperative day, accompanied by vigorous peristalsis, the gastric tube was removed. Small oral feedings of glucose water were started. Although the infant's clinical appearance continued to be good, a mild degree of partial intestinal obstruction persisted for about 10 days. This was indicated by occa-

Figure 1. Roentgenogram showing dilated stomach and multiple segments of distended bowel. Figure 2. Barium enema showing normal large bowel with reflux into ileum and dilated segments of small bowel.

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sional regurgitations of oral feedings and some hyperperistalsis. In addition, a roentgenogram of the abdomen revealed some dilated loops of bowel. This partial obstruction was believed to be due to edema in and about the anastomosis in the jejunum. On the sixteenth postoperative day, just prior to discharge, a roentgenogram of the abdomen revealed no distended loops of bowel. The infant was then taking full-strength milk formula feedings and she was gaining weight daily. Three or four normal stools were passed each day. Blood chemistry determinations continued to be within normal limits. She was discharged from the hospital in good condition on the nineteenth postoperative day.

FACTORS IN SUCCESSFUL TREATMENT

Early diagnosis soon after birth is essential for a favorable prognosis in any of these patients. If the diagnosis is not made in the first few days of life, these infants die of severe dehydration and electrolyte imbalance and/or from generalized peritonitis following rupture of the distended upper bowel. The diagnosis is based on the clinical and roentgenologic findings.

Congenital atresia of the small bowel should always be suspected when the tetrad of vomiting, abdominal distention, gastric waves and/or intestinal patterning, and small scanty mucoid stools is observed soon after the first feeding in the first day of life. The suspicion should be confirmed by roentgenologic studies.

Vomiting is the first and most important symptom calling attention to the condition. The time of its appearance depends on the site of obstruction. High obstruction in the duodenum and upper jejunum causes vomiting during or within a short time after the first feeding. Lower obstruction may not produce vomiting for a longer period of time and often not until after several feedings have been given. Once vomiting begins, it continues almost constantly. Except in rare patients in whom the atresia is above the ampulla of Vater, the vomitus is always bile-stained, of a fluid character in high obstructions, and malodorous with a fecal character in lower obstructions.

Abdominal distention develops soon after birth. It is confined to the upper abdomen in high, but is generalized in the lower obstructions.

Peristaltic waves are present at birth and persist until later when an adynamic ileus may occur. In duodenal and high jejunal atresias, gastric waves from left to right may be seen. In those lower in the intestine, intestinal patterning is seen.

Instead of normal shiny dark green meconium being passed, only small, faintly green mucoid stools are noted. The use of

Farber's test *(14)* is of aid in proving the existence of complete intestinal obstruction. The absence of cornified epithelial cells of the vernix caseosa in stained smears of stools signifies complete obstruction.

Roentgenologic studies of each patient should be made for confirmation and determination of the location of the obstruction. The presence of clinical findings with evidence of distended loops of bowel on plain roentgenograms of the abdomen indicates obstruction. Even when these fail to locate the site of obstruction, surgical exploration usually should be immediately carried out without resort to roentgenographic studies with contrast media. The use of the latter, though it will localize the site of the obstruction, is dangerous because the barium may become obstructive, and more important, swallowed barium may be regurgitated and then aspirated into the lungs. In most patients plain roentgenograms suffice to localize the obstruction. They should be taken with the patient in the upright position. Typically, duodenal or high jejunal obstructions are indicated by a greatly dilated stomach and a duodenum almost equally large; jejunal obstructions by several distended loops of small bowel; and ileal obstructions by multiple dilated loops throughout the abdomen. Barium enema is often useful in demonstrating whether the site of the obstruction is in the small or large intestine.

Preoperative care. Optimum condition must be attained for each patient prior to operation in order to minimize the operative risk, but this preparatory period must not be too long as an operation is indicated as early as possible.

Infants with atresia of the bowel present some degree of dehydration and prerenal uremia secondary to oligemia and poor circulation. Several types of electrolyte and acid-base imbalance may be present, depending on the site of obstruction. Patients with high obstructions have a hypokalemic, hypochloremic alkalosis, possibly associated with hypocalcemic tetany. The predominant loss of chlorides in the vomitus produces bicarbonate excess and metabolic alkalosis. The latter depresses the blood ionized calcium with ensuing tetany. Patients with lower obstructions have a hypokalemic, relative hyperchloremic acidosis. The predominant loss of the alkaline intestinal secretions produces a bicarbonate deficit with relative chloride excess and metabolic acidosis.

Probably the most important alteration in blood electrolytes is the loss of potassium. A low blood potassium occurs in all obstructions, whether high or low, producing a serious effect on the

(14) Farber, S.: Congenital atresia of alimentary tract; diagnosis by microscopic examination of meconium. J. A. M. A. 100: 1753-1754, June 3, 1933.

neuromuscular system and the heart. Attention must be paid to potassium balance in these infants by obtaining periodic blood chemistry determinations and ECG's.

In the work-up of these patients blood chemistry determinations, a blood count, crossmatching of blood for transfusion, and a urinalysis should be obtained immediately. Appropriate wide spectrum antibiotics are given parenterally. Determinations of the sodium, potassium, chlorides, nonprotein nitrogen levels of the serum, and the carbon dioxide combining power are essential to the formulation of proper solutions for parenteral administration. A polyethylene tube is inserted into an ankle vein exposed through a skin incision for use as a route of continuous intravenous administration of fluid during the preoperative, operative, and postoperative stages. Total daily amounts of fluids to be given are estimated on the basis of 150 cc. per kilogram of body weight, with an additional 100 cc. per kilogram of body weight when clinical evidence of dehydration is present. As there is almost always a renal shutdown, it is good procedure to give 10 percent dextrose in water while awaiting the reports of the emergency blood chemistry determinations. This promotes the return of renal function. When the laboratory reports are received, the indicated types and amounts of fluid are given. Whole blood transfusions, using 10 cc. per pound of body weight, are given when indicated.

The stomach is emptied and washed through a catheter which is left in place during the operation and is used postoperatively for attachment to a Wangensteen suction apparatus. When dehydration, shock, and electrolyte and acid-base imbalances have been corrected, the infant is taken to surgery.

Surgical technic. The diagnostic considerations and surgical treatment of these newborns differ from those employed in older children. Some of the technics which are useful in the older age groups may actually increase the mortality if employed during this period of life *(15)*.

Although local anesthesia may be used, open drop ether with a mask gives better relaxation and exposure. The surgical treatment of an obstruction due to congenital atresia is the establishment of a side-to-side anastomosis between the parts of the intestinal tract immediately above and below the site of the obstruction *(7)*. It is essential that the surgeon establish the fact that the lower segment of bowel is patent and not obstructed by other areas of atresia. A simple procedure for determining the continuity and patency of the lower segment of bowel is to inject

(15) Weiner, L. R., and Richmond, J. B.: Diagnosis of surgical conditions of newborn infant. J. Pediat. 36: 107-121, Jan. 1950.

normal saline solution into the lumen by the use of a fine needle and then watch the fluid pass into the lower colon.

The open type of anastomosis without the use of clamps is recommended. Two layers of sutures are preferred for the anastomosis using No. 0000 catgut for the inner layer and fine silk for the serosal layer; but if 2 rows of sutures tend to compromise the lumen of the bowel, a single layer of fine chromic catgut is sufficient *(8)*. The tissues are delicate and require the utmost care in handling to avoid injury that would nullify the results.

When the proximal portion of bowel has become gangrenous or has perforated, it must be resected before the anastomosis is performed. With the site of atresia above the ampulla of Vater, a gastrojejunostomy is the procedure of choice. For duodenal atresias below the ampulla of Vater, a duodenojejunostomy is the recommended procedure. For all other atresias of the small intestine a side-to-side anastomosis is preferred *(8)*.

Ileostomy or enterostomy alone leads to a severe loss of fluid followed by marked dehydration that cannot be controlled by the intravenous administration of fluids. Surgeons who have had a great deal of experience with this procedure do not believe that it offers any hope of clinical improvement but may aggravate the condition.

Postoperative care. Penicillin and streptomycin are injected intramuscularly every day for the prevention of infection. Constant gastric suction is performed through a gastric catheter by the use of a Wangensteen apparatus. Appropriate fluids and whole blood are given by continuous drip in the ankle vein, paying particular attention to potassium balance.

The manipulation of the bowel at operation always produces some adynamic ileus for from 24 hours to several days. The return of peristalsis is indicated by passage of stools and/or flatus and bowel sounds heard by auscultation. When peristalsis is believed to have returned, the catheter is removed from the stomach and oral feedings are started. Small amounts (from 4 to 8 cc.) of glucose water every 3 hours are given at first. If no vomiting occurs, a weak milk formula is substituted. When all feedings are retained, the amounts are gradually increased until the baby is taking the usual formula. Postoperative roentgenograms of the abdomen should be obtained periodically for confirmation that the obstruction has been corrected.

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LABORATORY STUDIES OF THE ISONICOTINIC ACID HYDRAZIDES IN TUBERCULOSIS[1]

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MATTHEW H. FUSILLO

RECENTLY a number of relatively simple chemical compounds have been demonstrated to possess bacteriostatic properties against *Mycobacterium tuberculosis*. This property has been shown in vitro, in the experimental animal, and in human subjects. These chemical substances include certain sulfones, thiosemicarbazones, and the amino salicylic acids of which para-aminosalicylic acid (PAS) is one. Of these agents only PAS has achieved clinical acceptance, but because of its low level of activity it is used as an adjuvant to streptomycin or in patients with streptomycin-resistant tuberculosis. Reports from various parts of the world concerning the therapeutic efficacy of these compounds have encouraged intensive research in many laboratories for other simple, active drugs useful in combating tuberculosis in man. The discovery of the tuberculostatic properties of the isonicotinic acid hydrazide compounds in the past few years appears to have justified this rigorous laboratory search.

We wish to present concepts that seem currently most contributory to an effective therapeutic regimen using the derivatives of the isonicotinic acid hydrazides. The role of the laboratory will be stressed.

McKenzie et al. (2) reported that nicotinamide markedly suppressed the spread of tuberculosis in mice. When nicotinamide was incorporated as from 0.5 to 0.75 percent of the diet, the tuberculostatic results were equal to about 1 mg. of streptomycin given 4 times daily over the same test interval. After more than 5 passages through mice there were indications of developing resistance. Investigations of similar compounds led to a study

(1) Walter Reed Army Hospital, Washington, D. C.

(2) McKenzie, D.; Malone, L.; Kushner, S.; Oleson, J. J.; and Sabbarow, Y.: Effect of nicotinic acid amide on experimental tuberculosis of white mice. J. Lab. & Clin. Med. 33: 1249-1253, Oct. 1948.

of the pyrazines of which pyrazinamide appeared to possess the most activity (3). In tuberculous infections of mice, pyrazinamide proved to have a therapeutic index of 500 and to be 7 times as active by weight as nicotinamide and several times as active as PAS. In more than half of the patients studied, the tubercle bacilli were either reduced or eliminated from the sputum, but there was a rapid emergence of highly resistant organisms in those with far advanced disease and cavitation.

The early clinical and limited laboratory studies with isonicotinic acid hydrazide (isoniazid) and its isopropyl derivative (IPH) were encouraging (4-22). Unfortunately, the first reports were released to the public without sufficient experimental data concerning susceptibility of human strains of *Myco.*

(3) Malone, L.; Schurr, A.; Lindh, H.; McKenzie, D.; Kiser, J. S.; and Williams, J. H.: Effect of pyrazinamide (aldinamide) on experimental tuberculosis in mice. Am. Rev. Tuberc. 65: 511-518, May 1952.

(4) Zieper, I., and Lewis, R. A.: Tuberculosis in Macacus rhesus treated with isonicotinylhydrazine. Quart. Bull., Sea View Hosp. 13: 12-16, Jan. 1952.

(5) Grunberg, E., and Schnitzer, R. J.: Studies on activity of hydrazine derivatives of isonicotinic acid in experimental tuberculosis of mice. Quart. Bull., Sea View Hosp. 13: 3-11, Jan. 1952.

(6) Selikoff, I. J.; Robitzek, E. H.; and Ornstein, G. G.: Toxicity of hydrazine derivatives of isonicotinic acid in chemotherapy of human tuberculosis; preliminary report. Quart. Bull., Sea View Hosp. 13: 17-26, Jan. 1952.

(7) Robitzek, E. H.; Selikoff, I. J.; and Ornstein, G. G.: Chemotherapy of human tuberculosis with hydrazine derivatives of isonicotinic acid; preliminary report of representative cases. Quart. Bull., Sea View Hosp. 13: 27-51, Jan. 1952.

(8) Bosworth, D. M.; Wright, H. A.; and Fielding, J. W.: Marsilid in treatment of tuberculous orthopedic lesions; preliminary report. Quart. Bull., Sea View Hosp. 13: 52-73, Jan. 1952.

(9) Fust, B.: Orientation with regard to antitubercular (rimifon). Schweiz. med. Wschr. 82: 333, Mar. 1952.

(10) Uehlinger, E.: First experiences with rimifon in experimental guinea pig tuberculosis. Schweiz. med. Wschr. 82: 335, Mar. 1952.

(11) Editorial: New antituberculosis drugs. J. A. M. A. 148: 1034-1035, Mar. 22, 1952.

(12) Grunberg, E.; Leiwant, B.; D'Ascensio, I. L.; and Schnitzer, R. J.: On lasting protective effect of hydrazine derivatives of isonicotinic acid in experimental tuberculosis infection of mice. Dis. Chest 21: 369-377, Apr. 1952.

(13) Grunberg, E., and Schnitzer, R. J.: Effect of hydrazine derivatives of isonicotinic acid on infection of mice with M. tuberculosis var. bovis. Yale J. Biol. & Med. 24: 359-365, Apr. 1952.

(14) Bernstein, J.; Lott, W. A.; Steinberg, B. A.; and Yale, H. L.: Chemotherapy of experimental tuberculosis. V. Isonicotinic acid hydrazide (nydrazid) and related compounds. Am. Rev. Tuberc. 65: 357-364, Apr. 1952.

(15) Lewis, R. A., and Zieper, I.: Tolerance of Macacus rhesus for isonicotinylhydrazines; preliminary report. Dis. Chest 21: 378-384, Apr. 1952.

(16) Steenken, W., Jr., and Wolinsky, E.: Antituberculous properties of hydrazines of isonicotinic acid (rimifon, marsilid). Am. Rev. Tuberc. 65: 365-375, Apr. 1952.

(17) Editorial. Isonicotinic acid hydradize. Lancet 1: 702-703, Apr. 1952.

(18) Robitzek, E. H., and Selikoff, I. J.: Hydrazine derivatives of isonicotinic acid (rimifon marsilid) in treatment of active progressive caseous-pneumonic tuberculosis; preliminary report. Am. Rev. Tuberc. 65: 402-428, Apr. 1952.

(19) Selikoff, I. J., and Robitzek, E. H.: Tuberculosis chemotherapy with hydrazine derivatives of isonicotinic acid. Dis. Chest 21: 385-438, Apr. 1952.

tuberculosis to these agents. Preliminary studies have shown the effective tuberculostatic properties of isoniazid and IPH against the H37Rv strain.

The recent observations of Steenken et al. *(23, 24)* demonstrated the in vivo development of resistance of *Myco. tuberculosis* to isoniazid in 4 of 6 patients with chronic cavitation. Karlson and Ikemi *(25)* showed that in 15 of 17 human strains of *Myco. tuberculosis* and 7 bovine strains of *Myco. tuberculosis,* resistance to isoniazid was developed 16 fold after 4 transfers of the organism on egg yolk agar containing the drug. Eleven colonies selected from gradient plates were resistant to isoniazid in "concentrations greatly in excess of those required to inhibit the great majority of tubercle bacilli in the original inoculum." Hobby and Lenert *(26)* noted that in a given population of *Myco. tuberculosis,* cells resistant to isoniazid were found in significant numbers. Syzbalski and Bryson *(27)* have reported that resistance to isoniazid was a "one step" resistance. This is comparable to the development of resistance to streptomycin as opposed to the step-wise development of resistance of bacteria to penicillin and the broad spectrum antibiotics. Pansy et al. *(28)* showed that the isoniazid resistance of BCG develops rapidly and is lost on serial subculture. Studies in this laboratory *(29)* have confirmed the foregoing and have shown that 13 of 15 human strains of *Myco. tuberculosis* which were considered sensitive

(20) Greenberger, M. E.; Greenberger, A. J.; Klein, M.; and Turell, M.: Chemotherapy of genitourinary tuberculosis with isonicotinic acid hydrazide; preliminary observations. New York State J. Med. 52: 1041-1042, Apr. 15, 1952.

(21) Birkhaug, K.; McGlynn, D.; and Clark, M. E.: Viability and dispersion of BCG inoculated subcutaneously in guinea pigs. Proc. Soc. Exper. Biol. & Med. 80: 64-66, May 1952.

(22) Executive Committee of the American Trudeau Society: Current status of isonicotinic acid hydrazide in treatment of tuberculosis. Am. Rev. Tuberc. 65: 649-652, May 1952.

(23) Steenken, W., Jr.; Meade, G. M.; Wolinsky, E.; and Coates, E. O., Jr.: Demonstration of increased drug resistance of tubercle bacilli from patients treated with hydrazines of isonicotinic acid. Am. Rev. Tuberc. 65: 754-758, May 1952.

(24) Steenken, W., Jr.; Meade, G. M.; Wolinsky, E.; and Coates, E. O., Jr.: Drug resistant tubercle bacilli from patients treated with isonicotinic acid hydrazides. (Correspondence) J. A. M. A. 149: 187, May 10, 1952.

(25) Karlson, A. G., and Ikemi, Y.: Occurrence of human type tubercle bacilli (H37Rv) resistant to isonicotinic acid hydrazide in culture not previously exposed to drug. Proc. Staff Meet., Mayo Clin. 27: 239-240, June 1952.

(26) Hobby, G. L., and Lenert, T. F.: Resistance to isonicotinic acid hydrazide. Am. Rev. Tuberc. 65: 771-774, May 1952.

(27) Szybalski, W., and Bryson, V.: Bacterial resistance studies with derivatives of isonicotinic acid. Am. Rev. Tuberc. 65: 768-770, May 1952.

(28) Pansy, F.; Stander, H.; and Donovick, R.: In vitro studies on isonicotinic acid hydrazide. Am. Rev. Tuberc. 65: 761-764, May 1952.

(29) Fusillo, M. H.; Wagner, B. M.; and Kuhns, D. M.: Relationship of streptomycin sensitivity of M. tuberculosis to action of derivatives of isonicotinic acid. To be published.

to streptomycin were resistant to isoniazid and IPH. A study of 29 organisms of varying degrees of resistance to streptomycin indicated no relationship between resistance to isoniazid and streptomycin.

Middlebrook *(30)* using Vallee bovine and R1Rv strains of *Myco. tuberculosis* detected naturally occurring resistant variants of the organisms to isoniazid. In addition, he re-emphasized that the selection of variants of tubercle bacilli resistant to chemotherapeutic agents can possibly be inhibited by simultaneous exposure of these organisms to drugs whose modes of action differ. Syzbalski and Bryson *(27)* reported that combinations of IPH, and streptomycin, neomycin, viomycin, Pas, or thiosemicarbazone against the tubercle bacilli were purely additive, and Ilavsky *(31)* reported a synergistic action between isoniazid and streptomycin.

DISCUSSION

The problem of the streptomycin resistance of *Myco. tuberculosis* is well documented. Resistance based on natural selection appears to account for the "one step" pattern noted in vitro and in vivo. This means that the temporal relationship of drug to bacteria is critical concerning the rate of emergence of resistant forms. Thus a relatively constant number of highly resistant cells may be isolated at one time over a wide range of concentration of the drug. PAS has been shown to delay the development of resistance to streptomycin, but in time the tubercle bacilli became resistant. In a similar manner, the organisms may develop PAS resistance.

It was not entirely unexpected to find naturally occurring strains of *Myco. tuberculosis* resistant to the derivatives of the isonicotinic acid hydrazides. Resistance to these compounds is apparently independent and in no way correlates with susceptibility of the tubercle bacilli to other agents. The clinician cannot assume that a streptomycin-sensitive strain is also isoniazid-sensitive or that the converse is true. For this reason before therapy is instituted the degree of susceptibility should be determined by standardized in vitro tests. Workers in this field acknowledge the limitations of the tests used to determine the sensitivity of *Myco. tuberculosis*. They serve, however, as a guide to the clinician for effective therapy.

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(30) Middlebrook, G.: Sterilization of tubercle bacilli by isonicotinic acid hydrazide and incidence of variants resistant to drug in vitro. Am. Rev. Tuberc. 65: 765-767, May 1952.

(31) Ilavsky, J.: Synergistic action of isonicotinic acid hydrazide and streptomycin in vitro. Am. Rev. Tuberc. 65: 776-778, May 1952.

CONCLUSIONS

Tubercle bacilli develop resistance to streptomycin and the derivatives of the isonicotinic acid hydrazides in a characteristic "one step" pattern covering a wide range of drug concentration. There is no relationship between the susceptibility of *Myco. tuberculosis* to streptomycin or to PAS and derivatives of isonicotinic acid. The synergistic and/or additive effect of isoniazid has not been completely evaluated. In vitro laboratory susceptibility tests are essential as a guide to rational therapy.

BOOK REVIEWS

Problems of Aging, Transactions of the Fourteenth Conference, September 7-8, 1951, St. Louis, Mo., edited by *Nathan W. Shock,* Chief, Section on Gerontology, National Heart Institute, National Institutes of Health and the Baltimore City Hospitals, Baltimore, Md. Sponsored by the Josiah Macy, Jr. Foundation. 138 pages; illustrated. Printed by Progress Associates, Inc., Caldwell, N. J., 1952. Price $3.

In this compilation, the knowledge of various scientific disciplines is applied to the problems of aging. The authors have attempted to elicit provocative discussions of the difficulties which are being encountered in research and practice.

The book is divided into 4 sections: (1) Biology and Medicine, introduced by John Esben Kirk; (2) Sociology, Psychology, Education and Religion, introduced by Robert J. Havighurst; (3) Economics, Employment and Welfare, with a statement of the problem by Wilbur J. Cohen; and (4) Medical Services, Hygiene and Housing, introduced by the late Joseph W. Mountin. This approach to the problem of aging is of interest to the physician. There is no index and the references are of little value to the medical practitioner. The approach is unusual, but this publication does not add particularly to the accumulated knowledge on the subject.—*Commander T. D. Cuttle, MC, U. S. N.*

Principles and Practice of Anesthesiology, by *Vincent J. Collins,* M. D., Director of the Department of Anesthesiology at St. Vincent's Hospital of the City of New York. 528 pages; 99 illustrations. Lea & Febiger, Philadelphia, Pa., publisher, 1952. Price $10.

The author has produced a text covering all the phases of anesthesiology rather than a reference book on one small segment of the field. The need for such a book has been evident for some time to those engaged in teaching, whether it be undergraduate students or residents. This volume will be of greatest value to the student and part-time anesthesiologist. As in any book of this kind,

there are personal opinions with which any one reviewer would disagree, but there is relatively little material presented that would not receive universal acceptance. A noteworthy feature is the excellent bibliography at the conclusion of each chapter.

—*Lt. Col. E. P. Shannon, Jr., MC, U. S. A.*

Essentials of Dermatology, by *Norman Tobias,* M. D., Associate Clinical Professor of Dermatology, St. Louis University; Assistant Dermatologist, Firmin Desloge and St. Mary's Hospitals; Visiting Dermatologist, St. Louis State Hospital; Fellow, American Academy of Dermatology and Syphilology; Diplomate, American Board of Dermatology and Syphilology; Visiting Physician in the Department of Dermatology at the St. Louis City Hospital. 4th edition. 596 pages; illustrated. J. B. Lippincott Co., Philadelphia, Pa., publisher, 1952.

This text has been prepared specifically for the general practitioner and the student. As such it is a very good reference for the many dermatologic conditions certain to have been unheard of by both categories of nonspecialist. As an introduction to the subject, each topical discussion is considered to be adequate, and not too verbose. It does not depress the beginner, as do more extensive texts, with a plethora of complicated prescriptions. Many eponyms are mentioned, a distinct aid to the neophyte, unfamiliar with this trick of the specialist.

The sections on nursing care appear for the most part to be directions for the office nurse to prepare the accouterments for physical examination and therapy. Little in the way of specific nursing directions is given.

From the dermatologic viewpoint, the histopathology is not sufficiently detailed for the student, who as a specialist must depend on his own diagnosis, if he expects more aid from his biopsy than the usual, "chronic dermatitis," furnished by the general pathologist. I object to the definition of dermatology as a branch of internal medicine. The speciality is concerned with many fields, such as histopathology, radiation, physical therapy, and pharmacology.—*Capt. C. D. Bell, MC, U. S. N.*

BOOK REVIEWS

Viral and Rickettsial Infections of Man, edited by *Thomas M. Rivers*, M. D., Director of the Hospital, The Rockefeller Institute for Medical Research. 2d edition. 719 pages; illustrated. J. B. Lippincott Co., Philadelphia, Pa., publishers, 1952.

This new edition has been enlarged, revised, pruned, brought up to date, and made more clinically useful than its predecessor. It meets a distinct need in the modern medical library and should be available for medical students, medical practitioners, public health and laboratory workers, and members of the military medical services, so that the information contained therein is readily accessible. It is not designed for the advanced worker with viruses and rickettsia. It carefully surveys the basic facts of the rapidly growing field of knowledge in this complex field. The expert organization of the book, the careful selection of material, the general clarity of style, the excellent documentation, both in chapter references and complete bibliologic and subject indexes, and the excellent illustrations, tables, and charts, make the volume easy to use.

Clinical material, including sections on epidemiology and control measures, is included throughout the book. The new chapter on the difficult subject of the diagnosis of viral and rickettsial infections should be of great value to the clinician. Other new chapters deal with human infections produced by the recently discovered Coxsackie viruses, viral hemagglutinins, and interference between animal viruses.

—*Lt. Col. W. R. deForest, MC, U. S. A.*

Veterans Administration Technical Bulletins, Series 10, Volume V, 1951. TB 10-71 through TB 10-81; illustrated. Veterans Administration, Washington, D. C., publisher, January 1952. Printed at Government Printing Office, Washington, D. C., 1952.

This book consists of 11 short monographs, each written by outstanding authorities: (1) "Parenteral Protein Nutrition" by Ravdin and Gimbel; (2) "Fever of Obscure Origin" by Beeson; (3) "Sarcoidosis" by Longscope; (4) "The Diseases of Collagen" by Baehr and Levitt; (5) "Cancer and Other Tumors of the Stomach" by North; (6) "Acute and Chronic Barbiturate Intoxication" by Isbell; (7) "The Management of Peptic Ulcer" by Ruffin; (8) "The

Differential Diagnosis of Vertigo" by Lindsay; (9) "Differential Diagnosis and Management of Pyogenic Meningitis" by Daniels and MacMurray; (10) "The Surgical Treatment of Cardiovascular Disease" by Hanlon; and (11) "The Management of Gastrointestinal Hemorrhage" by Elsom. These technical bulletins accurately and adequately cover all the essential points of interest to practicing clinicians. The method of presenting the material is almost identical with that used in the Department of the Army Technical Bulletins. This volume would be a valuable addition to any medical library or to that of any clinician interested in the subjects covered.—*Col. W. C. Berry, MC, U. S. A.*

Principles, Problems, and Practices of Anesthesia for Thoracic Surgery, by *Henry K. Beecher,* M. D., Henry Isaiah Dorr Professor of Research in Anesthesia, Harvard University; Director, Department of Anesthesia, Massachusetts General Hospital, Boston, Mass. American Lecture Series Publication No. 139, A Monograph in American Lectures in Anesthesia. 65 pages. Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $2.50.

This monograph for the practicing anesthesiologists is written in outline form with many subheadings. The major headings and divisions are somewhat confusing. The context, however, is explicit and the language is easily understood. Although almost half the book is devoted to the lobectomy-pneumonectomy group, very little new material is presented in this section. The author includes the generally known objectives concerning tracheobronchial secretions. The physical laws involved in coughing are reviewed and treatment to prevent troublesome coughing is discussed. Under the heading "Anoxia," positive pressure respiration is explained and the dangers are pointed out. Many of the finer points of positive pressure oxygenation are described and explained. Timely warnings are set forth and the physiologic basis for them is given.

The chapter entitled "Elevation of the Arterial Carbon Dioxide Tension" relates hypotensive states to increased alveolar CO_2 concentration quite well. Many questions are raised by the author as to the cause and possible remedy but they are left unanswered. In the circulatory section some excellent work has been done to correlate intrabronchial pressure with sudden and otherwise inexplicable drops in blood pressure. There is a notable lack of mention of apneic technics which are used by many anesthesiologists. The discussion of the maintenance of the circulating blood volume is not especially informative but points out some of the well-known phenomena that occur in relation to blood transfusions.

The discussion of the use of intratracheal tubes and inflatable cuffs in anesthesia for thoracic operations is excellent, but

there is little mention of direct connectors, types of aspirating catheters, or endobronchial intubation. Why controlled and assisted respiration should be included in the section on equipment is a mystery because it could well have been discussed in an earlier chapter. There is much evidence that controlled respiration has a definite place in anesthesia and for this reason should have been discussed more thoroughly. A discussion of the method of controlled respiration, rhythm, and correlation to blood circulation would have added much to a monograph of this nature.

Preanesthetic medication is considered here and the importance of atropine is emphasized. There are few who will support the author's routine use of quinidine preoperatively. The section on the choice of an anesthetic agent and technic ascribes little virtue to any agent but ether. That this view is fallacious is evident in the fact that a large percent of anesthesiologists use other agents quite satisfactorily.

In the section on the operative and postoperative care of the patient the author manifests a real concern for the patient and many of his points are well taken. There is some controversy as to the use of 100 percent oxygen as a "flushing" agent as this may cause postoperative atelectasis. Bronchoscopy when indicated and performed by a competent bronchoscopist is certainly invaluable. The section on the care of infants and children offers little that is new and is far too large a subject to be considered so briefly. The heading "Other Transthoracic Operations" contains many helpful suggestions.

This monograph is a handbook of anesthesia as practiced and taught by the author. His technics are apparently successful but his condemnation of other technics may lead to disagreement by other anesthesiologists.—*Lt. F. M. Thornburg, MC, U. S. N.*

Progress in Ophthalmology and Otolaryngology, A Quadrennial Review, Volume I, Part One, Ophthalmology, edited by *Meyer Wiener,* M. D., and *A. Edward Maumenee,* M. D. Part Two, Otolaryngology, edited by *Percy E. Ireland,* M. D., and *Joseph A. Sullivan,* M. B. 666 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., publishers, 1952. Price $15.

This book is a continuation of the idea which was conceived during World War II of reviewing "Ophthalmology in the War Years." It is divided into 2 parts; part 1 dealing with progress in ophthalmology between 1946 and 1950 and part 2 with the field of otolaryngology. All the phases of each field are covered in a concise but adequate manner by recognized authorities. A ready source of the current concepts of these fields is presented with an extensive bibliography.—*Capt. R. R. Powell, MC, U. S. N.*

Diseases of the Heart and Circulation, by *Albert A. Fitzgerald Peel*, M. A., D. M. (Oxon.), F. R. F. P. S. (G), Physician for Diseases of the Heart, Victoria Infirmary, Glasgow; Medical Consultant, Department of Health for Scotland and Ministry of Labour and National Service Recruiting Boards; Formerly Professor of Medicine, Anderson College of Medicine, Glasgow; Formerly Visiting Physician, E. M. S., Scotland. 2d edition. 472 pages; illustrated. Oxford Medical Publications. Geoffrey Cumberlege, Oxford University Press, New York, N. Y., publisher, 1952. Price $7.50.

This introduction to the study of cardiovascular disease is the outgrowth of a series of lectures to medical students given by the author. The new edition incorporates recent advances in the knowledge of cardiovascular physiology which has resulted from phonocardiography, angiocardiography, and cardiac catheterization, without becoming involved with the details of these technics. The incorporation of new material has necessarily lengthened the book. Clinical methods available to the general practitioner are stressed. The first 94 pages are devoted to a detailed discussion of history taking, physical examination, and roentgenographic studies of patients with cardiovascular diseases. The discussion of cardiac findings in roentgenographic and fluoroscopic studies is particularly good, and the text is illustrated by excellent roentgenographic plates. Traumatic cardiovascular lesions are well covered. Discussion of the common types of heart disease is thorough.

Certain viewpoints expressed in this work will meet with some opposition in this country. The author believes that quinidine has an undeserved reputation for conversion of paroxysmal tachycardias, making no distinction between supraventricular and ventricular tachycardias in this regard. Auricular fibrillation and flutter are explained on the classic "circus movement" theory. The author finds few indications for conversion of auricular fibrillation to normal rhythm, and believes that for this reason the use of quinidine is contraindicated in long standing fibrillation, and absolutely so in patients with a history of former embolism. He recommends fluid restriction as well as sodium restriction in the treatment of cardiac failure. Although anticoagulant therapy is introduced in this edition, only one paragraph is allotted to the technic of its use, and the author does not mention the need for a prothrombin determination prior to the administration of the initial doses of dicumarol or tromexane.

As a whole, this book achieves the author's objective. It will continue to be of value to medical students and practitioners as an introduction to cardiology, and will serve well those who desire a brief review of the subject.

—*Col. B. E. Pollock, MC, U. S. A.*

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